4-79

# 1979 Program Highlights

U.S. DEPARTMENT OF
HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

Division of
Research Resources

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# 1979 Program Highlights

## Division of Research Resources

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# Introduction

In this time of inflation and rising research costs, the provision of shared research resources is critical to the continuance of productive biomedical research. Through its five programs, the NIH Division of Research Resources (DRR) supports the development and maintenance of resources—advanced tools, materials, specialized environments for research, expanded capability for ethnic minority faculty and students, and improved quality for biomedical science.

The Division currently supports 75 clinical research centers, 7 primate research centers, over 46 animal research resources, 47 biotechnology resources, and 80 minority biomedical support grantees. In addition, it provides funds to enhance the research capability of qualified research institutions and individual investigators through more than 450 Biomedical Research Support Grants. Since the advancement of biomedical research depends on investigators' access to research resources, the Division strategically locates its resources in institutions across the country, so that a large and diverse group of biomedical scientists can share them.

The purpose of this publication is to describe the activities during 1979 in each of the Division's programs and to highlight the resulting research progress in areas of national health concern.



READEX MICRO

# Report of the Division Director

During 1979, grant awards were made to 795 institutions in the amount of $149,926,000. Seventy-five General Clinical Research Centers (GCRC's) were supported, including 613 research beds and 76,042 outpatient visits, which represented 80 percent of research inpatient care for the NIH Institutes. Forty-seven biotechnology resources were funded and made available to a number of investigators across the country. The facilities housing these resources were frequently the scene of productive encounters between experts in a given technology and experts in a particular medical discipline. Core support of seven Primate Research Centers enabled 145 center staff scientists to conduct research on 214 projects and provided 504 collaborative and affiliated scientists from various academic institutions with the opportunity to conduct research on 136 projects.

In addition, the Division's Biomedical Research Support Grant (BRSG) Program provided funds to 457 institutions to purchase needed equipment, to train new investigators, to develop pilot projects, or for research needs not appropriately funded by Public Health Service (PHS) project grants or other sources. These awards supported 4,467 regular research projects, as well as 5,098 pilot projects to strengthen basic research.

Many more ethnic minorities entered schools or professional training in biomedical research as a result of the DRR Minority Biomedical Research Support Program. Positions funded included 739 undergraduates, 247 graduate students, and 402 faculty.

By developing, supporting, and providing research resources to the nation's biomedical investigators, the Division substantially strengthened and advanced biomedical research in 1979 and made a positive impact on national health. The following were a few of the variety of substances, techniques, and treatments developed or tested using DRR-supported resources in 1979:

- A cholesterol-lowering, low-calorie artificial fat.
- Mechanical insulin pump to regulate the flow of insulin into the body.
- A guinea pig model of diabetes mellitus.
- A treatment to detoxify the body of Kepone and other pesticides.
- A bioautofuel cell to transform the energy of the body's biochemical reactions into electricity to power microelectronic implanted devices such as the cardiac pacemaker.
- Computer programs which simulate the thought processes of clinical experts, to aid in the diagnosis and treatment of certain diseases.
- An improved method for preserving blood platelets for transfusion.
- A unique data base designed to elucidate the molecular basis and genetic control of antibody specificity.

There are many more individual examples of research highlights within each program section.

The Division also accomplished important management and administrative goals set for 1979:

- Streamlined the Division's computerized information system to:
  - —Monitor NIH research projects to determine their resource needs.
  - —Track DRR grant and contract operations.
  - —Evaluate DRR program progress.
- Expanded the number of Minority Biomedical Support interagency agreements with NIH Institutes to support minority activity needed for Institute-funded research projects, thus strengthening the research efforts of the individual Institutes.
- Developed or improved several mechanisms to ensure cost-effective use of Division funds:
  - —A management workshop for new GCRC administrative coordinators and three regional meetings with BRSG program directors.
  - —An expenditure plan to identify continuing obligations and planned procurements for each quarter.
  - —Improved financial forecasting methods.
  - —Automated budget formulation and justification processes.

In addition, the Division increased its response to the information needs and concerns of its biomedical research constituency and the lay public. Through its Research Resources Information Center, contracted under the direction of the Division's Office of Science and Health Reports (OSHR), the DRR advised researchers, through its award-winning *Research Resources Reporter* (circulation 14,000), where research resources could be located and how they could be used in research and informed them of the latest advances in biomedical research. The Division also provided information in its directories of animal, biotechnology, and clinical resources, as well as minority biomedical support.

During the year, the OSHR organized and participated in numerous national, local, and regional communications projects to inform the public about research activities at DRR-supported biomedical research resources. The office also distributed 34,822 publications. Another major OSHR publication project was the revised edition of *NIH Primate Research Centers: A Major Scientific Resource*, which won the American Medical Writers Association first-place award for booklets/brochures for professional audiences.

These achievements and others cited in this report demonstrate the effectiveness of DRR administrative efforts and attest as well to the strength of its five diversified research resource programs.

Thomas G. Bowery, Ph.D.
Director, Division of Research Resources
National Institutes of Health

**FY 1979 Division of Research Resources Budget**

| Program | Appropriation | Major Resources Supported |
|---|---|---|
| General Clinical Research Centers Program | $ 51,848,000 | • 75 General Clinical Research Centers<br>• Over 3,000 Research Projects<br>• Research Physician Development Program |
| Biotechnology Resources Program | $ 14,269,000 | • 47 Biotechnology Resources<br>— 18 Computer Resources<br>— 2 Biomedical Engineering Resources<br>— 25 Instruments for Biological Structure and Function<br>— 2 Cellular and Biochemical Material Resources |
| Animal Resources Program | $ 23,654,000 | • 7 Primate Research Centers, including 214 Core Research Projects<br>• 11 Primate Breeding Projects<br>• 84 Animal Research and Resource Project Grants and Contracts<br>• Training Programs |
| Minority Biomedical Support Program | $ 14,584,000 | • 80 Institutions<br>• 500 Research Projects<br>• 402 Minority Faculty, 739 Undergraduates, and 247 Graduate Students |
| Biomedical Research Support Program | $ 44,952,000 | • Biomedical Research Support Grants to 457 Institutions<br>• 5,098 Pilot Research Projects<br>• 4,467 Regular Research Projects<br>• Central Resources<br>• Development Awards to 32 Institutions |
| Program Management/ Direct Operations | $ 4,762,000 | |
| Total Budget | $154,069,000 | |

# General Clinical Research Centers Program

## Program Description

Although some animals and in vitro models can simulate human biological systems and disorders, eventually it becomes necessary to submit promising findings and procedures to clinical study. Moreover, a large number of human maladies exist only in man and cannot be modeled at all. Ultimately, there is no substitute for a direct study of the intact human organism, i.e., clinical research.

This realization led the U.S. Senate in 1959 to urge special studies on humans and to authorize establishment by the NIH of Clinical Research Centers. Eight centers were created in 1960 from a $3 million appropriation. The number of centers had grown to 60 when the NIH Division of Research Resources (then the Division of Research Facilities and Resources) assumed responsibility for the General Clinical Research Centers Program in 1962.

The objective of the GCRC Program is to establish and make available to medical scientists the specialized clinical environment necessary to conduct high-quality clinical research. To accomplish this objective, the program supports, via competitive grants, General Clinical Research Centers. Each center is a miniature hospital-within-a-hospital with the specialized equipment and expert personnel to provide a multidisciplinary, controlled research environment.

Today, there are 75 centers throughout the country, where scientists study the entire spectrum of biomedicine from genetics to organ transplants. Their research projects are funded by NIH and other agencies of the Department of Health and Human Services, by research foundations and societies, and by industry.

A typical center functions as a discrete unit within a hospital. Most centers contain approximately 8 beds, but the range is from 4 to 30. Each GCRC consists of a core laboratory, a metabolic kitchen, treatment rooms, a patient lounge area, a nurses' station, a conference room, and an outpatient section. The core laboratory and the metabolic kitchen provide the controlled environment necessary to study complex disease processes.

Biomedical research often requires that a patient's diet be strictly monitored for weight, chemical composition, and caloric value. Standard hospital kitchens, subject to heavy workloads and often lacking specialized equipment, cannot provide the precise measurements necessary for research. GCRC metabolic kitchens are equipped to make these measurements, and they serve also as training facilities for dietetic interns and graduate dietitians. Similarly, valid research results are dependent upon laboratory tests conducted with costly, sophisticated analytical equipment rarely found in standard hospital laboratories. GCRC core laboratories provide the specialized equipment and trained staff needed for clinical studies.

The GCRC staff is as specialized as its facilities. A typical center supports 1 or 2

## Overview of the GCRC Program 1969—1979

| FY | Centers | Full-Time Positions Funded | Funded Beds | Inpatient Days[1] | Outpatient Visits | Apportionment |
|---|---|---|---|---|---|---|
| 69 | 93 | 2,298 | 1,023 | 245,943 | — | $35,004,000 |
| 70 | 93 | 2,076 | 904 | 244,824 | 1,175 | 35,004,000 |
| 71 | 82 | 1,885 | 881 | 234,870 | 14,515 | 38,004,000 |
| 72 | 84 | 1,867 | 907 | 238,152 | 23,654 | 42,181,000 |
| 73 | 83 | 1,790 | 893 | 227,501 | 36,280 | 41,300,000 |
| 74 | 87 | 1,795 | 877 | 232,534 | 50,614 | 42,320,000 |
| 75 | 84 | 1,732 | 823 | 223,269 | 50,020 | 42,619,000 |
| 76 | 84 | 1,727 | 784 | 222,488 | 56,217 | 42,533,000 |
| 77 | 82 | 1,679 | 755 | 204,369 | 65,130 | 47,283,000 |
| 78 | 79 | 1,706 | 633[2] | 193,151 | 70,588 | 51,946,000 |
| 79 | 75 | 1,622 | 613[2] | 198,000 | 76,042 | 51,848,000 |

[1] Includes research and nonresearch patients
[2] Excludes 73 nonresearch beds

medical program directors, as well as 12 nurses, 3 dietitians, 2 laboratory technicians, and some administrative personnel.

The combined capacity of the 75 centers is equivalent to that of a 600-bed hospital devoted entirely to clinical research. In addition to facilities for adult patients, GCRC's also provide the unique care needed in pediatric studies. Currently, 110 of the research beds are on pediatric wards or in children's hospitals, and 70 of the centers admit pediatric patients on a regular basis. One center is devoted to studying health problems of perinatal care, and another focuses on the health problems of premature infants.

## Program Growth

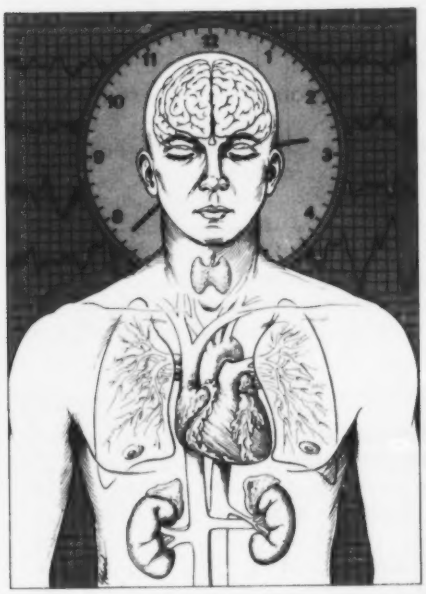
This year the GCRC's conducted approximately 3,000 research projects and supported 80 percent of the NIH-supported inpatient research care costs for studies performed outside the NIH campus. Despite a decrease in the number and size of the centers, the GCRC Program is more productive now than it was 10 years ago. This progress resulted from significant changes designed to cope with two trends threatening clinical research progress: 1) rapid increase in costs of hospitalization (13 percent per year) and hospital personnel (9 percent per year); and 2) the declining number of physicians who remain in research rather than pursue careers in clinical practice.

To deal with these problems in a direct manner, the program initiated in the early seventies a service patient policy, created outpatient facilities at the centers, and instituted a clinical associate physicians (CAP) awards program.

The service patient policy requires that third-party insurers reimburse the centers for those patients sick enough to require hospitalization (about one-third of center patients). The centers continue to pay all research-related costs for those patients and all costs for patients hospitalized primarily for research. This policy alone has saved the program $10 million each year.

During the 1970's, outpatient facilities were created at the centers. Unused bed space was converted to examining rooms, and center personnel were retained to provide logistical, nursing, and dietary support for outpatient research studies. These studies have been particularly useful for research in clinical pharmacology and in chronic metabolic conditions where periodic followup rather than continual monitoring is needed. Outpatient research has grown vigorously from 1,175 outpatient visits in 1970 to 76,042 in 1979.

*There is no substitute for a direct study of the intact human organism through clinical research. This research is best conducted within the controlled environment of DRR-supported General Clinical Research Centers.*



*GCRC core laboratories provide the specialized equipment and trained staff needed for clinical studies. Here a researcher performs biochemical analyses of patient blood samples within a GCRC core laboratory.*

*A researcher uses a Biostator to monitor the metabolic readings of a GCRC diabetic patient, while it systematically infuses insulin into the patient. In 1979, the 75 DRR-supported General Clinical Research Centers conducted 80 percent of such NIH-supported inpatient research performed outside the NIH campus.*

To attract talented young physicians to research careers, the program initiated the CAP program in 1973. This program is designed to help train an expert national core of clinical investigators. It provides attractive and stable salaries for physicians to engage in clinical research at a center for up to 3 years. In 1979, 30 CAP positions were funded. Of the first 40 CAP's who completed the program, 36 are continuing in research careers.

Other significant achievements that contributed to a more productive program in 1979 were:

☐ Inpatient admissions increased during the past 10 years from 23,000 to 30,000, and inpatient research publications increased, despite a decrease in the number of program-supported centers.

*A biomedical scientist examines a cell culture used to determine the degree of enzyme deficiency in a patient with a degenerative eye disorder. The controlled environment of GCRC's makes such precise research possible.*

☐ Continued development of an urgently needed computer-based data management system, CLINFO, enabled clinical investigators to collect and analyze large amounts of research data.

☐ Two nationally shared core laboratory resources for clinical applications of mass spectroscopy were developed.

☐ The mixed center concept was implemented, which permits nonresearch patients to use uncommitted GCRC beds to reduce center operating costs.

☐ Communication among centers, with the NIH, and with national organizations of program directors, research nurses, dietitians, and administrative coordinators improved. This trend was reinforced by publications and services of the DRR Office of Science and Health Reports and those of the Research Resources Information Center.

These administrative achievements, coupled with intensified review by institutional and national review systems during the seventies, have resulted in the high quality of research reflected in the 1979 research highlights.

## Program Highlights for the Year

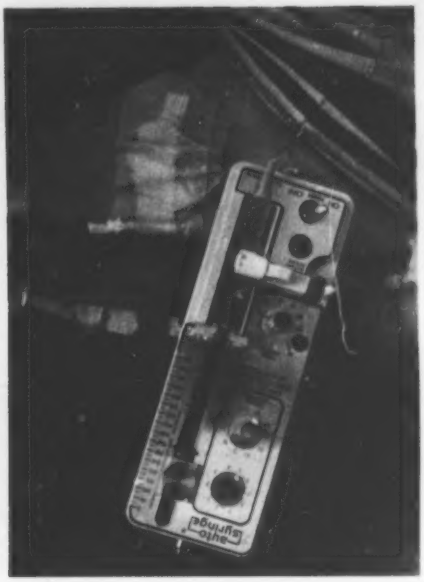
The approximately 3,000 research projects conducted at the centers this year reflected national health concerns and research initiatives of the various NIH Institutes. In 1979, the GCRC program supported 433 center projects in nutrition at a cost of $10,150,000; 578 projects on genetics costing $7,242,000; 330 projects on diabetes costing $5,962,000; and 91 projects on arthritis costing $1,540,000.

Some of the techniques that were tested and developed at the GCRC's during 1979 promise to improve national health by advancing prevention, diagnosis, treatment, and cure of disease. They are discussed in detail below.

### Artificial Fat

Sucrose polyester is an artificial fat that can be synthesized to resemble corn oil or any semisolid shortening. When added to food, this artificial fat appears to be a safe, effective, noncaloric, well-tolerated substance that significantly reduces blood cholesterol levels regardless of cholesterol content in the diet. The compound does not change the consistency of the food containing it and is currently being tested in 120 GCRC outpatients. It also holds promise for retarding or preventing atherosclerosis, a form of hardening of the arteries that has been linked to elevated levels of dietary cholesterol.

*Wearable, automatic insulin pumps regulate the flow of insulin into the body. The pumps, which mimic the output of a normal pancreas, were tested in diabetic patients at two GCRC's this year.*



**Insulin Pump**

Two new wearable, automatic insulin pumps are being tested at two GCRC's. Each is the size of a paperback book and can inject insulin under the skin of a diabetic person at rates that mimic the output of a normal pancreas. With these pumps, fluctuations in blood sugar are considerably less than when insulin is administered by the usual method of one or two manual insulin injections per day. This more precise control of blood sugar levels may prevent or delay the onset of the complications of diabetes such as kidney failure, blindness, and peripheral vessel disease. More sophisticated versions of one of these pumps would be completely implantable and remotely controlled by the patient, with no wires or tubes breaking the skin. These later versions may also involve glucose sensors for automatic feedback control of the blood sugar.

**Prenatal Diagnosis of Thalassemia**

Thalassemia, a debilitating blood disease that occurs predominantly in Mediterranean people, can now be detected prenatally by a newly discovered technique. This technique detects different forms of thalassemia by identifying hemoglobin genes in fetal cells taken from amniotic fluid. It may also be applicable to prenatal diagnosis of conditions such as immunoglobulin disease, sickle cell anemia, hemophilia, or other genetic conditions that affect a large number of Americans.

**New Antihypertension Drug**

Captopril, a new antihypertension drug investigated during 1979 in GCRC research, acts by blocking formation of the potent blood-pressure-raising hormone angiotensin II. Captopril can lower blood pressure in many patients with either renovascular hypertension due to kidney failure or essential hypertension, which is resistant to multiple combinations of other drugs.

**Lyme Arthritis**

GCRC research this year led to new findings on tick-borne arthritis. It was discovered that a different tick than originally thought carries the disease. The disease is similar to rheumatoid arthritis but has a characteristic skin lesion and includes neurologic involvement in the early stages. Studies are currently under way to determine the etiologic agent carried by the tick. The ticks involved feed on a variety of animals, but the presence of household pets, particularly cats, increases the risk of exposure.

**Diagnosis of Connective Tissue Diseases**

The development of new diagnostic tests at a GCRC this year has enabled clinicians to diagnose more accurately patients with any one of several rheumatological conditions. these tests can distinguish patients who have mixed connective tissue disease, a relatively benign and manageable condition, from patients with the more serious disseminated lupus erythematosus, which requires intensive therapy. These tests are the result of years of research which involved serological examination of thousands of serum specimens and observation of hundreds of patients.

**GCRC Research Publications**

The growing number of GCRC research accomplishments and medical advances are reflected in the 50 percent increase in published GCRC research since 1971. In 1971,

research on inpatients resulted in 2,219 publications, with 246 originating from outpatient research. In 1978, there were 3,345 publications, including 1,130 involving outpatient research. (Data for 1979 are not yet available.)

## Future Program Directions

GCRC scientist administrators believe that in the 1980's the program will face increased demand for use of GCRC beds, a greater need for CLINFO (a computer-based, clinical data management system), more need for sophisticated core laboratory analytical devices, and a continued declining interest by young physicians in research careers. The program plans to meet these needs by providing more research beds, expanding the CLINFO system, placing sophisticated technology in center core laboratories, and continuing its CAP program for physicians.

**More Research Beds**

The increased demand for use of GCRC beds will stem from stepped-up research initiatives by the NIH in areas of national concern, mainly chronic and degenerative diseases. More than 90 percent of NIH-supported investigators will be examining problems related to heart disease, hypertension, kidney disease, diabetes, cancer, child health, and stroke. However, fewer than 5 percent of them will have hospitalization or patient care costs included in their NIH awards. Therefore, they and other investigators will need access to controlled clinical facilities like the GCRC's in order to apply knowledge gained in their basic research to the prevention, control, and treatment of human illnesses. Investigators at a growing number of medical schools and research institutes will also need GCRC bed space.

To meet these needs, the GCRC Program plans to continue to promote high-quality inpatient and outpatient facilities at existing centers during the 1980's.

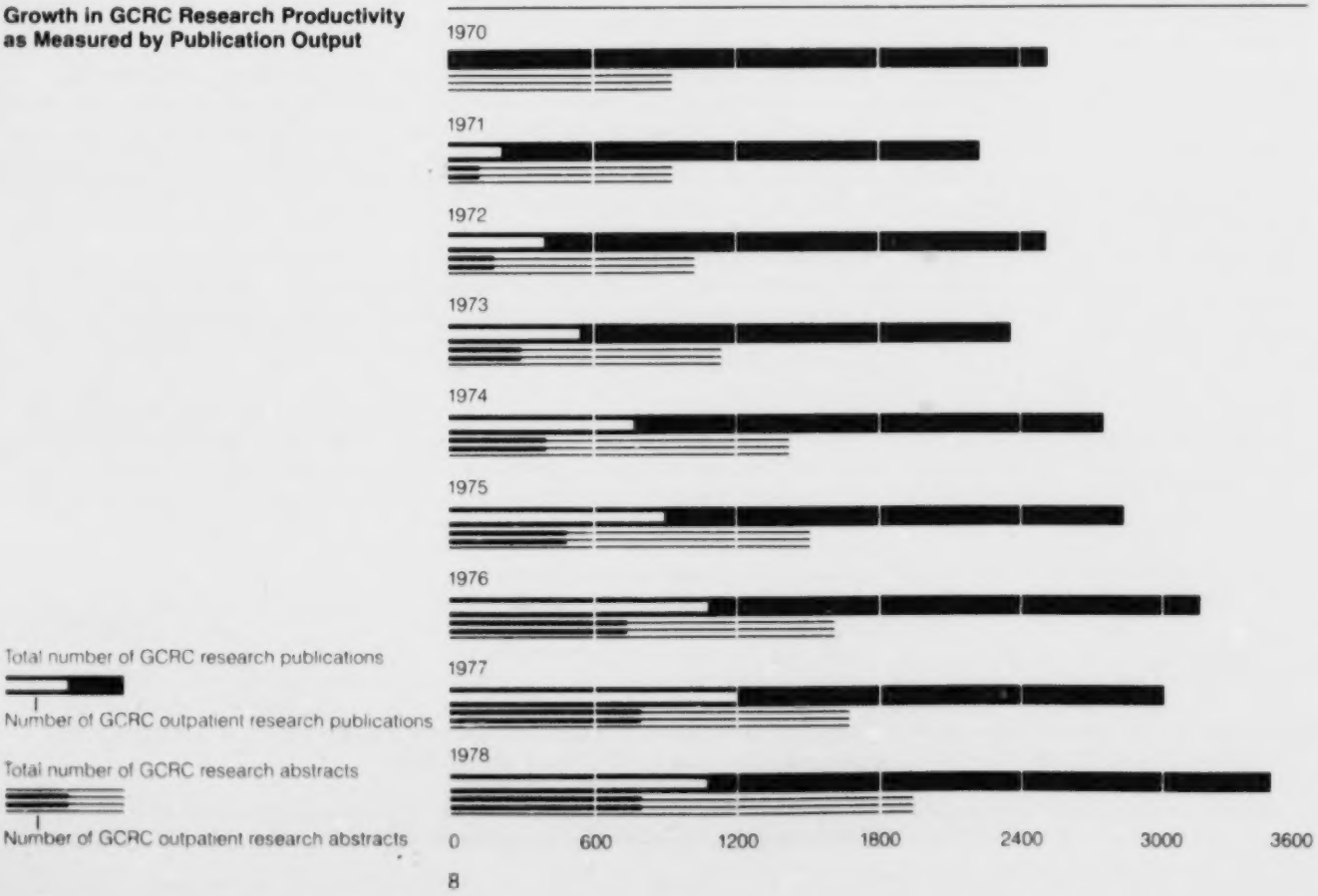
**Diffusion of CLINFO**

With clinical research data continuing to increase in complexity and amount, more centers will need access to CLINFO to process and analyze large quantities of research data. To meet this need, the GCRC Program will diffuse CLINFO to more GCRC's in the decade ahead.

**Placement of Core Laboratory Technology**

Future efforts to upgrade the quality of clinical research must include continual refinement

**Growth in GCRC Research Productivity as Measured by Publication Output**



*A video display unit and hard copy device, which constitute a typical terminal of the CLINFO computer-based data management system. By enabling clinical investigators to collect and analyze a large amount of research data, CLINFO contributed to more productive GCRC research in 1979. The program plans to extend use of the CLINFO system to more GCRC's in the eighties.*

of measurement and testing techniques. To meet this requirement for precision, investigators need sophisticated laboratory technology with broad applicability to a number of clinical research protocols. For example, high-pressure liquid chromatography allows metabolic studies of proteins, fats, steroids, drugs, hormones, and intermediary metabolites with use of one instrument. Since this type of technology is expensive and requires technical skills not usually included in the training and work experience of physicians, its location in a core laboratory with trained personnel could enhance future clinical research. To meet this need in the eighties, the GCRC Program will introduce technologies appropriate for clinical investigation to core laboratories at selected centers and make these available to as many centers as possible.

**Continuation of the CAP Program**

Laboratory technology and use of CLINFO can enhance the quality of clinical research, but this research cannot continue without an expert core of clinical investigators to translate basic research into improved health care. To maintain the nation's corps of expert clinical investigators, the GCRC Program will continue its successful CAP program.

Finally, the GCRC Program will strive to extend the use of these centers to more and more researchers in the eighties. The improved use and operation of these pooled national resources holds the promise for important future advances in patient care and disease prevention.

*The GCRC Program plans to upgrade clinical research in the 1980's by increasing access by investigators to such sophisticated measurement and testing technology as mass spectroscopy. Two nationally shared core laboratory resources for clinical applications of mass spectroscopy were supported by the program in 1979.*

# Biotechnology Resources Program

## Program Description

Biomedical research has advanced so rapidly that some scientists today cannot move further in their fields of investigation without the aid of new biotechnology. For example, instruments that image and analyze the structure and function of proteins, nerve cells, and nucleic acids, or implantable miniature sensors that can measure the temperature of lesions or the level of oxygen in the blood, enable researchers to sharpen the focus of their investigations. For many scientists, these instruments are the door from the known into the unknown.

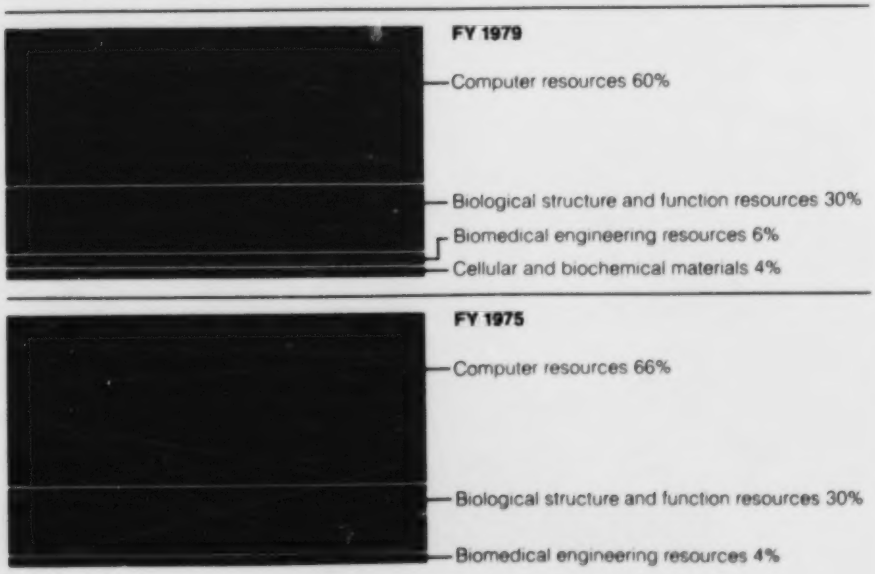
Biotechnological advances began to accelerate in 1962 when the NIH initiated a specialized research equipment program, now the DRR Biotechnology Resources Program (BRP), at the suggestion of Congress. The purpose of the program is to support and develop technologies needed to solve biomedical and clinical research problems.

Biotechnology resource facilities provide a unique opportunity for experts in particular technologies to collaborate with experts in the biomedical sciences to advance the nation's health. The three major types of resource facilities supported by the program include: specialized, large-scale and minicomputer centers; bioengineering facilities that apply engineering knowledge and technology to produce biomedically useful products; and facilities that house instruments for analyzing and characterizing biological structure and function, e.g., mass spectrometers, million-volt electron microscopes, and nuclear magnetic and electron spin resonance spectrometers. The program provides grants for establishing and maintaining these resources, and it awards research contracts for adapting technological capabilities developed in the commercial sector for use by the biomedical community.

The program's main objective is to use comprehensive engineering skills and facilities to create biomedically relevant technologies and to make these technologies accessible to as many biomedical scientists across the country as possible.

In 1979, the program budget of $14.5 million supported 47 resources and 4 resource-related research projects. Several of the resources are national in scope, and each is characterized by five specific research functions: core research, collaborative research, service, training, and information dissemination. Core research is research done at the resource facility to develop and apply the technology. Often an on-site expert in the technology helps a user with a new and difficult application. Such collaborative research sometimes results in expanding not only the application of the technology, but

**Percentage of the DRR Biotechnology Resources Program Budget Funded for Each Type of Biotechnology Resource in FY 1979 Compared to FY 1975**



also the depth of the research study. In order to retain program support, biotechnology resource facilities must also encourage use of the resource. The facilities inform users of the availability and application of the resource by information dissemination, and core technology experts train and assist them in its use. By allowing a large group of investigators to share these expensive resources, the program has greatly reduced the national cost of biomedical research.

Increased sharing of these resources has been achieved by strategically locating them according to national use patterns and by selecting for development those technologies most needed by the NIH and other U.S. biomedical research scientists.

*Researchers monitor operation of a Scanning Transmission Electron Microscope (STEM) from the control room. This instrument, visible through the window (center), enables scientists to relate the chemical properties of molecules to their three-dimensional structure. In 1979, the Biotechnology Resources Program supported 47 resources.*

Program-supported biotechnology was used during 1979 for 663 research projects of 11 NIH Institutes and for 128 projects of several Public Health Service agencies such as the Alcohol, Drug Abuse, and Mental Health Administration, the Food and Drug Administration, and the Health Resources Administration.

Since the beginning of the program, the technological level and focus of these resources have kept pace with the increasingly sophisticated needs of biomedical researchers. Originally supporting large, general computer centers in medical schools, the program has diversified its resources to embrace an extremely broad and innovative array of biomedically relevant technologies.

## Program Growth

### Computer Resources

The computer facilities currently supported by the program bear little similarity to the conventional computer centers of the past. Today's computer systems are far more specialized, more compact, more capable, and less expensive. In addition to providing sophisticated numerical computing and information-processing services, present systems apply artificial intelligence methodology to clinical decision making, interpret molecular structures, and image protein structures and nerve cells in three dimensions.

The most controversial biomedical computer innovation of the last decade, and one with potential to revolutionize health care in the eighties, is the application of artificial intelligence methodology to clinical diagnosis. Until recently, attempts to design intelligent machines for medical application met with indifferent results or with failure. Within a few years, however, a computer program that mimics the reasoning process used by physicians may be able to analyze and diagnose many of the major diseases of internal medicine. This system, INTERNIST, already contains a major portion of the knowledge applicable to internal medicine, translated into mathematical bytes and stored in the computer memory. The computer holds a profile for each disease in its memory. When completed, the system will be able to assist both physicians seeking advice on difficult medical problems and paramedics serving in remote or medically underserved areas. Another recently developed computer system, CASNET/Glaucoma, can greatly facilitate the diagnosis, prognosis, and prescription of treatment for patients with glaucoma. The end product of medical judgment, knowledge, and engineering, these prototype computers are the experimental bridge between the judgment of the expert and the treatment chosen by the practitioner.

### Biomedical Engineering Resources

Biomedical engineering resources have increased in sophistication and range of application. One of the current foci of biomedical engineering is development of miniature sensors and implant devices. One sensor, smaller than a needle, can be inserted into breast cancer lesions to measure temperature distribution within the lesion during microwave therapy. Another, when inserted in blood vessels, analyzes blood chemistry (pH, oxygen, and carbon dioxide) in the bloodstream. The most recent product of this application of microelectronic technology to biomedicine is the bioautofuel cell mentioned earlier. Further research is needed to develop materials compatible with the body's chemistry for housing these devices.

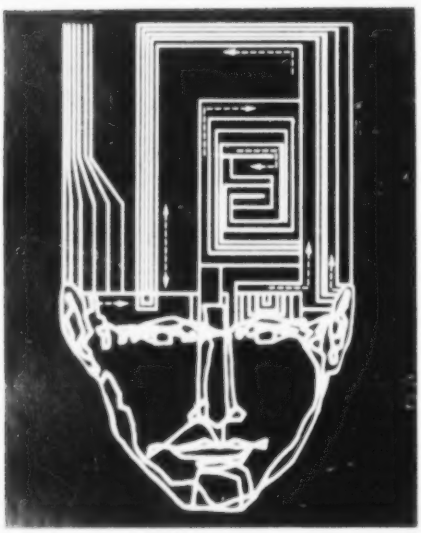
### Instrumentation for the Study of Biological Structure and Function

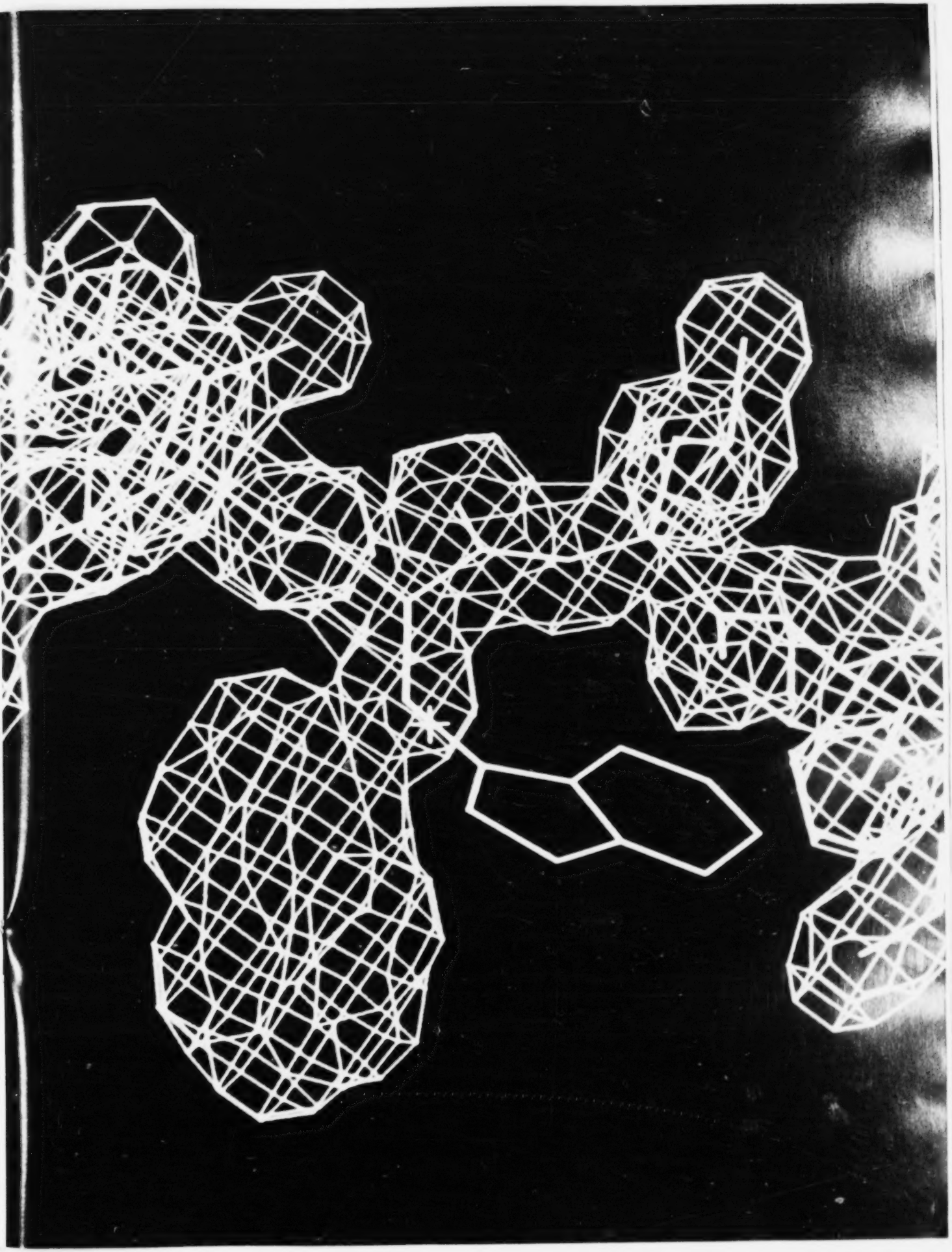
Program-supported resources that assist investigators in characterizing the structure and function of biological substances include facilities for mass spectrometry, nuclear magnetic resonance (NMR) spectrometry, electron spin resonance spectrometry, electron microscopy, and biomedical kinetics.

Program-supported facilities continually update the state of the art and broaden the applications of these different technologies. In one research project, investigators have developed new instruments and computer methods to expand the biomedical applications of mass spectrometry, generally used to identify unknown substances. As a result, mass spectrometry was combined with gas chromatography into a unique system capable of identifying drugs in body fluids in less than an hour, thus enabling the identification of drug overdoses in coma victims. Further development of mass spectrometry may eventually enable biomedical scientists to detect diseases prior to clinical manifestations.

In collaboration with the National Science Foundation, program-supported scientists have enhanced the functions of NMR spectrometers by the introduction of higher resolution (500 to 600 MHz) instruments. The NMR spectrometers with a higher field can distinguish signals from large biomolecules such as proteins and nucleic acids that are blurred at lower fields of spectrometric analysis. As a result, they promise to provide researchers with new understanding of the structure and function of these large molecules.

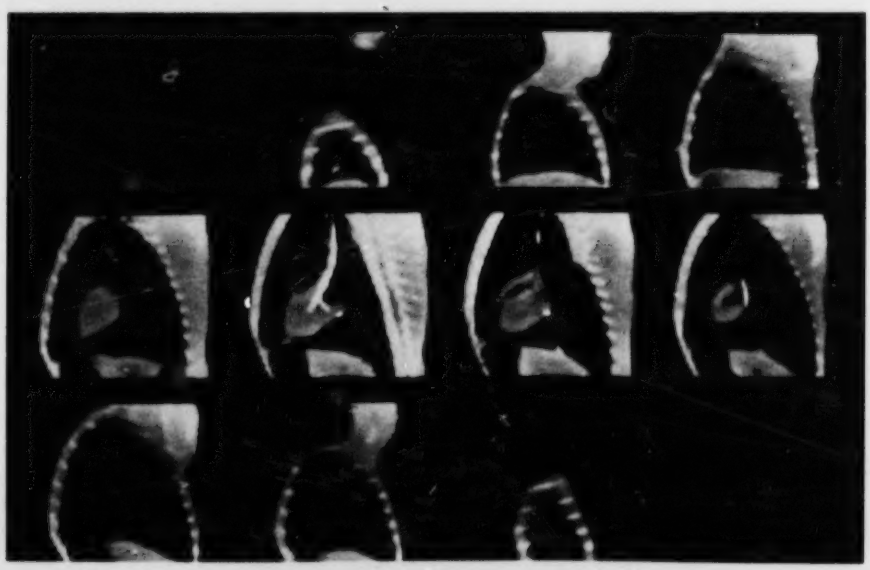
## Program Highlights for the Year





*A micrograph of a fractured chicken eggshell, magnified 1,200 times, shows the resolution of a scanning electron microscope. Such instruments for the study of biological structure and function are often a researcher's door from the known into the unknown and can broaden the scope of research.*

*The dynamic spatial reconstructor, developed with DRR and National Heart, Lung, and Blood Institute grants, is a body-imaging device scheduled for clinical use in 1980. Here it images separate thorax sections, each 3 mm thick. Pictures begin at the left body wall, moving through the chest to the right wall.*

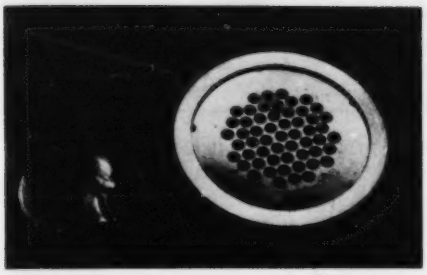


☐ Workshop on hearing loss to explore use of technology and biomedical engineering to ameliorate hearing problems.

☐ Workshop to discuss technical computer science issues involved in the clinical applications of artificial intelligence, notably the computational mechanisms in the INTERNIST II system.

☐ Workshop to introduce experts in the field of biomolecular structure to the first version of CONGEN, a series of interactive computer programs that assists scientists in exploring potential structures of unknown compounds.

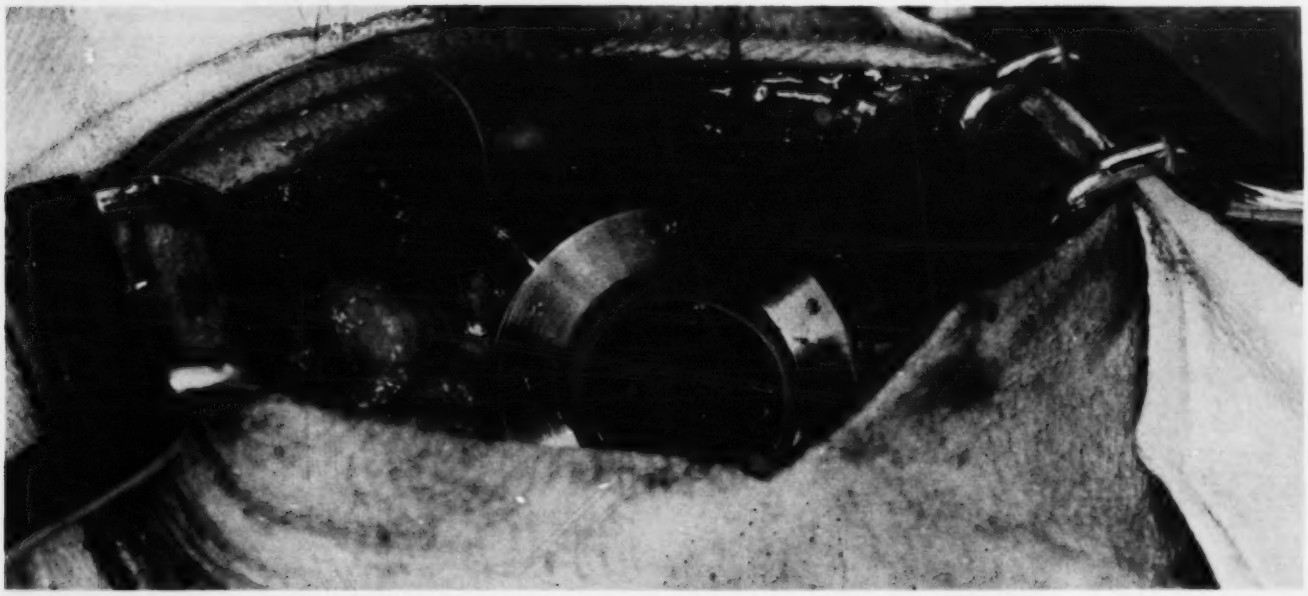
☐ Symposium to dedicate a new regional nuclear magnetic resonance facility. Emphasis was on use of NMR to study glycoproteins, protein dynamics, conformation of mobile peptides, tRNA, biological membranes, and the red blood cell.



The contribution of biotechnology in advancing biomedical research is evidenced by the 1979 research accomplishments of the resource facilities, including development of a dynamic spatial reconstructor, development of an implantable bioautofuel cell, and use of PROPHET to elucidate the molecular basis of antibody specificity.

**Dynamic Spatial Reconstructor (DSR)**

This imaging device will soon be tested at a biotechnology computer facility. Recently developed with grant support from the DRR Biotechnology Resources Program and the National Heart, Lung, and Blood Institute, it produces rapid serial section images of whole body sections 20 times larger than those possible with more conventional imaging devices. Scheduled for experimental clinical use in 1980, it provides stop action, slow motion, and elapsed-time movie displays of the functioning heart, lungs, and circulatory system. Using the DSR, each section of the heart can be isolated on film and observed as it beats. Since so much pathology is associated with the mechanism of interaction between tissues and the circulatory system, the DSR promises an advanced aid in the prompt diagnosis and treatment of many diseases.



*One of the current foci of biomedical engineering resources supported by the Biotechnology Resources Program is development of miniature sensors and implantable devices such as this bioautofuel cell. Barely larger than a quarter, it powers microelectronic implant devices such as the cardiac pacemaker by generating electricity from the body's chemical reactions. It is currently being tested in laboratory animals (above).*

**Bioautofuel Cell**

This device, slightly larger than a quarter, transforms energy of the body's chemical reactions into electricity to power implanted microelectronic devices such as the cardiac pacemaker. A battery-powered telemetry system was developed at a biomedical electronics resource facility in 1979. It was wired to the bioautofuel cell, which was implanted for testing in animals. After further testing, the cell may eventually be used in humans to power cardiac pacemakers, implanted devices which regulate blood pressure, or those which monitor glucose levels in the body.

**Molecular Basis of Antibody Specificity and Its Genetic Control**

Joint 1979 investigations by BRP-supported researchers using the PROPHET system created a unique data base designed to elucidate the molecular basis and genetic control of antibody specificity. This data base contains virtually all published sequences of immunoglobulins and their activity. Such knowledge is essential to any area of biology and medicine in which an organism's immune system may play a role in combating—or in some cases, in causing—disease or dysfunction. The data base has proved so valuable

that it has been published and distributed worldwide through a DRR publication *(Sequences of Immunoglobulin Chains,* NIH Publication No. 80-2008).

Other significant 1979 research highlights include:

- ☐ Further development of a new technique for medical imaging, zeugmatography, which uses a magnetic field and radio waves to produce images of internal tissues and organs.
- ☐ Development of a computerized genetic counseling system.
- ☐ Development of a computer model using artificial intelligence to describe the disorder of paranoia.
- ☐ Production of the first large volumes of nearly pure carbon-13 isotope for use in pharmacological research.
- ☐ Detection of vitamin B-12 deficiency in children, using a mass spectrometry resource.
- ☐ Confirmation of the structure of fibrinogen, a protein essential to blood clotting, at a scanning transmission electron microscope facility.

## Future Program Directions

In the 1980's, program administrators believe, the program will continue to face escalating costs, obsolescence of biotechnology equipment, and the increasing need for these resources. To offset the costs of supporting the resources most needed by biomedical scientists and of introducing promising new technologies, the program will encourage mature resources to become self-supporting via user fees or other funding sources. The program will also use workshops, as it did this year, to determine the need for and uses of evolving technologies and to make these resources accessible to as many biomedical scientists as possible. Finally, the program will continue to focus its support on computer technology, biomedical engineering, and instrumentation for the study of biological structure and function.

Computer resources will explore the use of microcomputers, which are rapidly becoming as powerful and capable as minicomputers yet are less expensive and more compact. Recent software and hardware developments in microcomputer technology are heading toward lightweight, low-cost, battery-powered portable systems. One computer facility is already developing a microcomputer device for rehabilitating patients with muscular impairment due to strokes and accidents, and a microcomputer-based stimulator has been developed for basic and clinical research on the visual system. Also on the agenda for the eighties are exploration of computer networking, the application of very large scale integrated circuit technology, and the continued development of artificial intelligence into a number of clinical decision-making systems.

*An artist's rendering of the transformation of expert judgment into a computer program for clinical diagnosis. The continued development of artificial intelligence methodology into clinical decision-making systems will be supported by the Biotechnology Resources Program in the 1980's.*

Biomedical engineering resources will continue to develop new, useful devices for monitoring physical and chemical reactions in the body. Recent advances in high technology associated with solid-state sensors should facilitate development of a valuable system to monitor these reactions in vivo. Exploration of microsensor technology and tissue-compatible biomaterials will also be a focus of research in the eighties.

Instruments for the study of biological structure and function will be continually updated as more applications are discovered. The interfacing of liquid chromatography with mass spectrometry is already being practiced at several resources to produce an instrument which can separate most biological compounds. Similarly, new applications for NMR spectrometry, electron microscopy, and biomedical kinetics will be pursued. Other resources to be developed in this area include pulse laser technology, synchrotron radiation, and acoustic imaging microscopy.

# Animal Resources Program

## Program Description

Animals are an extensively used research resource. Approximately 30,000 to 35,000 primates are needed annually for U.S. biomedical research, and over half of the research projects supported by the NIH require animals. To meet the research demand for well-nourished, disease-free animals with known genetic backgrounds, as well as the demand for animal maintenance facilities, the Division of Research Resources established its Animal Resources Program (ARP) more than 15 years ago. Today the program supports seven Primate Research Centers (PRC's), numerous primate breeding and supply projects, specialized animal models and colonies, and a variety of other animal research projects. It is a major source of animal models and specimens used by U.S. biomedical researchers and is comprised of three subprograms: the Primate Research Centers Program, the Primate Breeding and Resources Program, and the Laboratory Animal Sciences Program.

**Primate Research Centers Program**

As early as the mid-1940's, U.S. scientists were concerned about the scarcity of nonhuman primates and of facilities for research. By 1961, the PRC Program had been initiated by the NIH to establish specialized facilities where biomedical scientists could study primates to learn about human health-related problems. Within 5 years, seven centers had been completed, forming the largest network of its kind in the world. Located to serve the broadest research community, the centers are in Beaverton, Oregon; Seattle, Washington; Southborough, Massachusetts; Atlanta, Georgia; Madison, Wisconsin; Covington, Louisiana; and Davis, California.

Each center has a primary research focus. Taken together they comprise research areas that can be carefully studied in nonhuman primates:

☐ *Neurophysiology, mental retardation, communicative disorders, learning disorders, and developmental behavior*—Primates are especially valuable in these studies because of their highly developed nervous system.

☐ *Reproductive biology and population control*—The primate reproductive system is anatomically and physiologically more similar to the human system than is that of other animals.

☐ *Cardiovascular diseases*—The response of the primate cardiovascular system to nutrition and stress is similar to that of humans.

☐ *Infectious diseases*—Certain primate species are uniquely susceptible to some human diseases, such as hepatitis.

☐ *Environmentally induced and chronic diseases*—Primates are well suited to studies of these health problems, which generally involve multiple body systems and require an animal model that resembles man in toto.

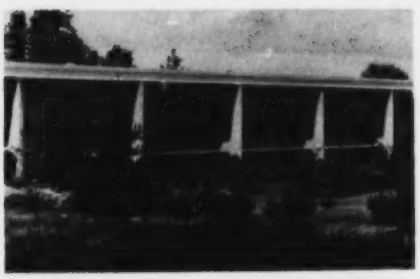
Primate center operations are supported by core grants awarded by the DRR Animal Resources Program to the host institution or to foundations that serve as grantee institutions. The host or grantee institution is responsible for management of the funds. At the beginning of the PRC Program, 2-year grants were awarded to cover land acquisition, architectural fees, and construction costs for the centers. Currently, peer-reviewed, 5-year grants support administrative, operational, and core research costs, including salaries of the core staff.

**Primate Breeding and Resources Program**

Natural populations of primates have gradually declined as their habitats have been disrupted and destroyed. As a result, all primate species today are classified by the Convention on International Trade in Endangered Species as either clearly endangered or likely to become so. Countries which once exported thousands of primates annually to the United States no longer do. In 1973, a total of 69,548 primates were imported into the United States, 79 percent of which came from India, Thailand, Bangladesh, Peru, and Colombia. Currently, however, because of conservation efforts, none of these countries allows commercial export of nonhuman primates. The rhesus monkey, long a standard laboratory primate, is now virtually impossible to import, yet at least 2,400 rhesus

*The Primate Breeding and Resources Program supports breeding colonies to assure an adequate supply of primates for U.S. biomedical research. This primate enjoys the open environment of a free-ranging breeding colony in Key Lois, Florida.*

*Research on the rhesus monkey (opposite page) at the Yerkes Regional Primate Research Center indicates that this primate may provide a useful model for studying cystic fibrosis. The DRR Animal Resources Program supports the development and maintenance of the animals and facilities essential to such important animal research.*



*The main research building at the Oregon Primate Research Center, which contains modern laboratories, surgical suites, and animal care facilities. The seven Primate Research Centers annually provide over 1,200 biomedical scientists with a specialized environment for the study of nonhuman primates.*

*The DRR Laboratory Animal Sciences Program funds improvement projects at research institutions to upgrade animal facilities. Funds are usually used for animal cages, general sanitation equipment such as the cage-washer (above), renovation of animal facilities, and salaries of trained professional and technical personnel.*

monkeys are needed each year for NIH extramural research alone. Cynomolgus monkeys have been used to replace rhesus in many projects, and approximately 2,250 cynomolgus monkeys are needed annually for NIH extramural research.

To offset these shortages and to ensure a supply of research primates to U.S. biomedical scientists, the ARP funds the Primate Breeding and Resources Program, whose specific objectives are to:

- ☐ Breed domestically those commonly used primate species that cannot be obtained from wild population supplies.
- ☐ Carry out research on primate breeding and development of domestic primate populations.
- ☐ Conduct ecological, behavioral, and other field studies to gain basic knowledge for cropping or selectively harvesting national primate populations.
- ☐ Conduct studies directed toward conservation of research primates.

During the past 5 years, the program funded fewer primate resource projects and more primate supply projects, including six projects for domestic breeding of rhesus, cynomolgus, and squirrel monkeys. The ARP also continues to support a Primate Supply Information Clearinghouse that facilitates the exchange of primates and tissues among investigators, thus conserving primates.

**Laboratory Animal Sciences Program**

In the mid-1960's, the ARP established the Laboratory Animal Sciences Program (LASP) to provide biomedical scientists with healthy, high-quality, research animals. The LASP supports a number of activities designed either to improve the quality of animals used in biomedical research or to enhance the availability of animals with special characteristics as research models.

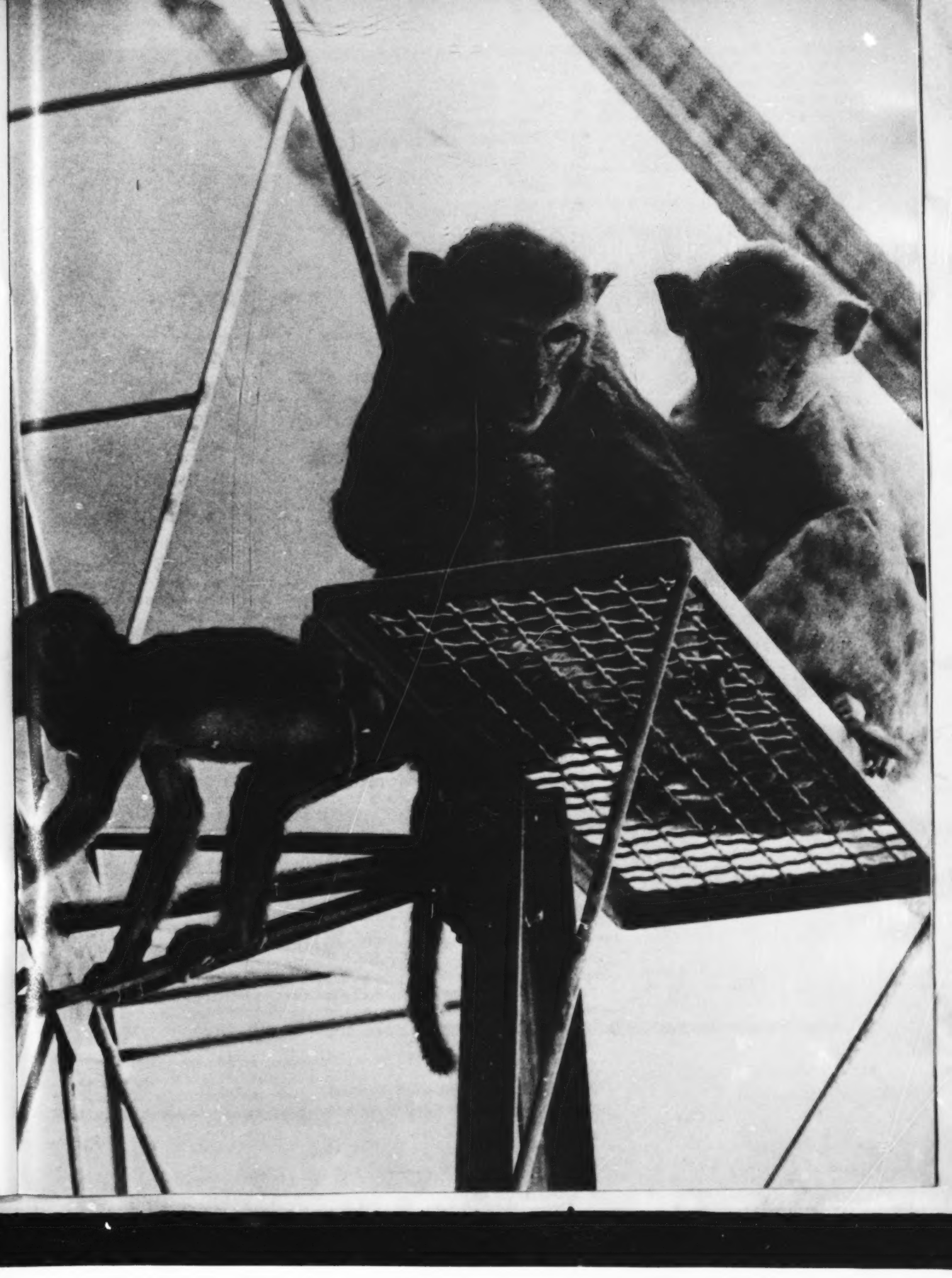
As the LASP evolved, its support for different projects shifted. Grants for institutional improvements were the main funding thrust in the early 1970's, peaking at 55 percent of awarded LASP funds in 1974. During the past 5 years, as turnover in improvement projects slowed, more LASP dollars were awarded to other program components. Currently, support is distributed evenly among animal models, special colonies, and resource laboratories, which together account for about 70 percent of LASP funds.

***Institutional Animal Resource Improvements.*** Improvement projects are supported to help institutions upgrade their animal facilities and develop centralized programs of animal care. Funds are usually used for animal cages meeting current regulations, general sanitation equipment such as cage-washers, renovation of animal facilities, and salaries of trained professional and technical personnel. Projects are supported for 1 to 3 years, after which the institution is expected to assume financial responsibility for its basic animal resource. Over the past 7 years, 89 institutions have received improvement grants totaling approximately $11.5 million.

***Animal Models and Special Colonies.*** Many experiments to understand human growth, metabolism, and disease require specific genetically and environmentally controlled animal models. Primates, for instance, develop a better replica of human atherosclerosis than rabbit models. Similarly, Old World primates, with menstrual cycles resembling that of humans, offer a good model for studying the physiology of human reproduction. Specifically, the objectives of these projects are: 1) to define, characterize, and exploit the relevant biological attributes of selected animals that display potential for use in biomedical research; 2) to establish, improve, or expand special colonies of well-characterized animals of proven value for biomedical research that are not generally available from other sources; and 3) to preserve unique and valuable stocks and strains of animals that might otherwise be lost.

***Resource Laboratories.*** Resource laboratories have been a major program activity for over 10 years. Most resource laboratories are institutional in nature, but some serve more than one institution in a metropolitan or regional area. The total number of laboratories supported (13 to 15) has remained relatively constant in recent years, although the institutions receiving awards have changed. The 15 laboratory programs currently supported, including a new laboratory funded in 1979, represent 20 percent of the LASP budget. The objectives of these laboratories are: 1) to provide for improved animal health programs through investigation of naturally occurring diseases and related laboratory animal problems; 2) to support studies resulting in new information on diseases of laboratory animals and their etiology; 3) to aid in discovering new laboratory animal models of human disease; and 4) to develop resources, including tissues, slides, and photographs, for research and training.

***Resource-Related Research.*** Projects are funded to investigate the etiology, pathogenesis, and control of laboratory animal diseases and to determine the environmental requirements of laboratory animals. Support of resource-related research has been accorded a very high priority by the Animal Resources Review Committee



*National Research Service Awards supported by the Animal Resources Program provide investigators with training that enables them to professionally care for laboratory animals such as the newborn primates in the nursery (right).*

because of the widespread recognition among laboratory animal specialists that naturally occurring animal diseases and environmental factors can invalidate research results. The absence of careful qualitative control can produce erroneous data.

***Training.*** Training in laboratory animal science prepares individuals to provide professional care of laboratory animals, to manage central animal resources, and to give special assistance to investigators through knowledge of laboratory animal biology and research methods. Trainees are also prepared to participate in teaching graduate students and young investigators and to pursue their own research either independently or in teams. Since the inception of LASP grants and fellowships, approximately 148 trainees and fellows have completed training; most of them (usually 10 to 12 per year) remain in the field of laboratory animal medicine.

***Reference Centers and Information Projects.*** The Laboratory Animal Sciences Program also supports several centers and information projects, including the Registry of Comparative Pathology, which provides consultation, publications, training, and research focused on comparative pathology; a Blood Group Reference Laboratory, which provides nonhuman primate blood typing; an Animal Model Reference Center with a sperm bank for animal models; and publication of the *Laboratory Primate Newsletter.*

## Program Highlights for the Year

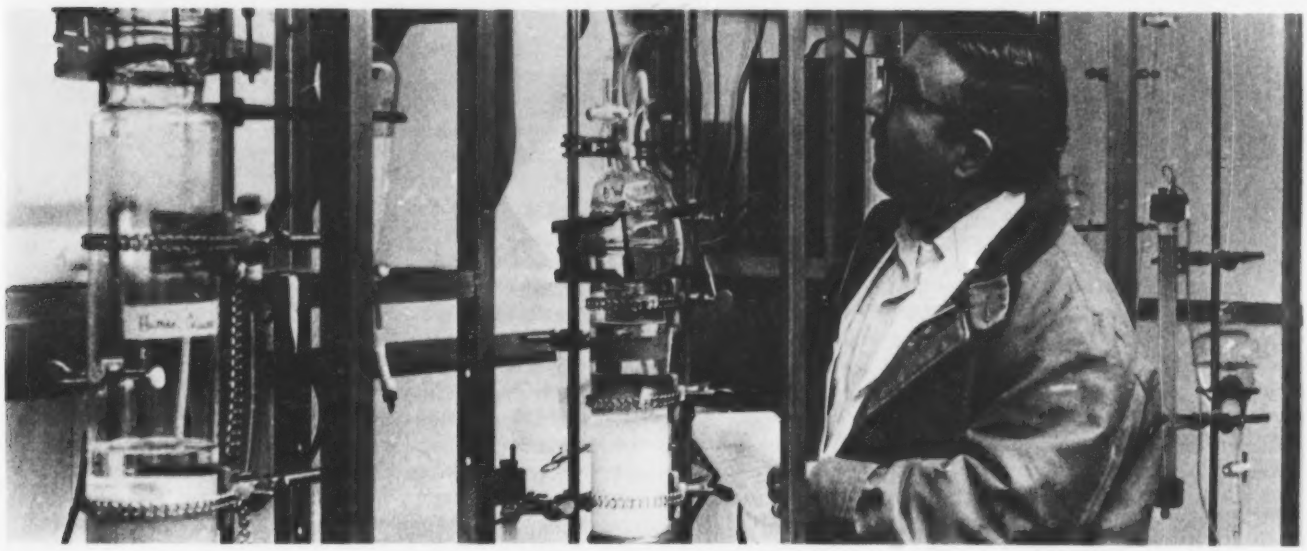
Several significant trends in 1979 challenged the Animal Resources Program. Primate supply became critical this fiscal year when Bangladesh and other countries stopped exporting nonhuman primates. Therefore, the program increased its domestic breeding efforts. The year 1979 also marked an increased recognition among laboratory animal specialists that naturally occurring laboratory animal diseases and environmental factors can adversely affect research results. As a result, resource-related research to upgrade the health and environment of laboratory animals was accorded high priority. A third priority was the renovation of deteriorating animal resource facilities. Fewer institutional improvement projects were funded in recent years, enabling the program to fund new projects and to combat inflationary costs.

Finally, 1979 was marked by two administrative initiatives: evaluation of both the Primate Research Centers Program and the overall national status of animal resources and development of a long-range plan for animal resources. Evaluation of the Primate Research Centers Program was conducted by a panel of nine distinguished scientists

*An immunologist surveys instrumentation at the Division of Immune Diseases laboratory in the Oregon Primate Research Center. During 1979, specialized instruments and other research services of the seven Primate Research Centers were made available to 504 collaborative and affiliated scientists.*

and scientist-administrators. The panel visited each center and surveyed other primate resources. All seven centers were evaluated for location, size, research focus, organization, NIH policy guidelines, and funding levels. A comprehensive survey of laboratory animal facilities and resources provided up-to-date information on the nation's animal resources available for biomedical research. Conducted under contract by the Institute of Laboratory Animal Resources, National Research Council/National Academy of Sciences, the survey encompassed areas of animal resource costs, administration and personnel, facilities and equipment, and animal sources and use. Both final evaluation reports have been completed.

Recommendations from both evaluations will be considered in developing the



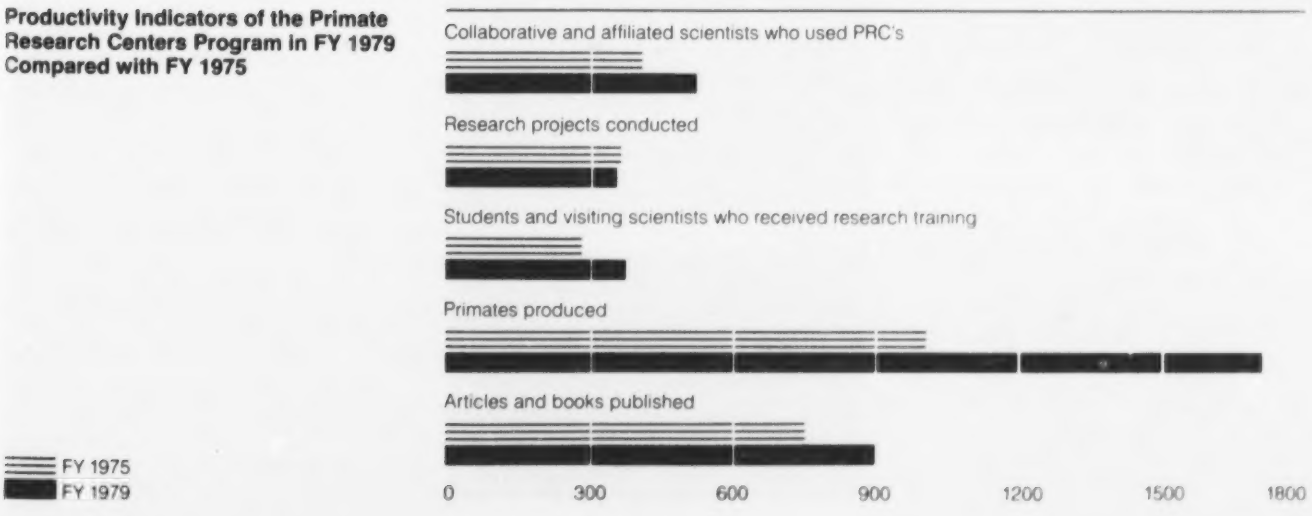
long-range plan for animal resources, which was initiated this year in conjunction with an overall DRR planning effort.

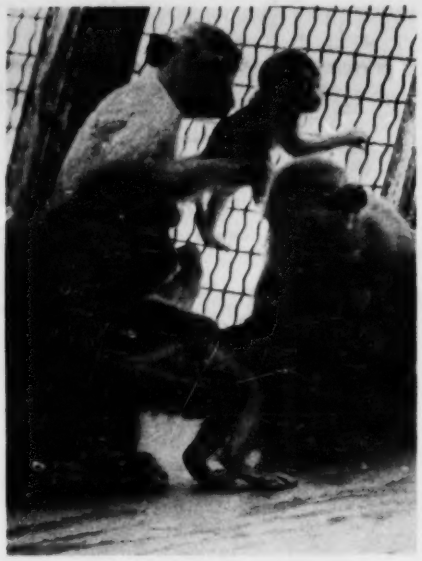
Following are 1979 highlights for individual areas of the Animal Resources Program.

**Primate Research Centers Program**

During 1979, the program supported seven Primate Research Centers with $15.24 million in grants. The centers' 145 core staff investigators conducted research on 214 projects. These research projects were funded by approximately $3.9 million from 103 NIH research grant/contract awards and $1.5 million from other Federal and non-Federal agencies. The resources and services of the centers were made available to 504 collaborative and affiliated scientists who conducted research on 136 projects supported by $3.7 million from NIH grants and contracts and $700,000 from other sources. PRC research resulted in over 900 published journal articles and books by the core staff, collaborators, and affiliated scientists.

**Productivity Indicators of the Primate Research Centers Program in FY 1979 Compared with FY 1975**





*During 1978–79, two social behavior studies at the Wisconsin Primate Research Center investigated maternal-infant behavioral relationships, including maternal adoptions of infant primates. Here an adult female rhesus monkey (left) with no infant of her own grooms and fondles an infant without incurring protest from the nursing mother.*

The centers also conducted research training for 215 graduate students and 33 visiting scientists, provided salary support for 675 technical and administrative staff personnel, and supplied over 7,700 biological specimens to 328 scientists.

Special emphasis continued to be placed on domestic breeding of those primate species most widely used in center research projects. In 1979, the centers bred approximately 60 to 65 percent of their requirements, as well as maintaining small nuclear colonies of less commonly used species to assure their survival for future research needs.

Research conducted at the Primate Research Centers in 1979 included:

- ☐ A study of the lung tissue of premature infant monkeys to determine the basic causes and pathophysiology of respiratory distress syndrome, the leading cause of infant death in the United States.
- ☐ A study of spontaneous diabetes in *Macaca nigra*, which may lead to a useful tool for diagnosing impending diabetes before clinical signs appear.
- ☐ Studies on the responses of nonhuman primates to general anesthetics and to inhaled environmental pollutants.
- ☐ Research on the immunology of malignant melanoma, with production of an antibody to successfully identify human melanoma cancer cells.
- ☐ Studies on aging which suggest that cellular pigment may be linked to the aging process.

**Primate Breeding and Resources Program**

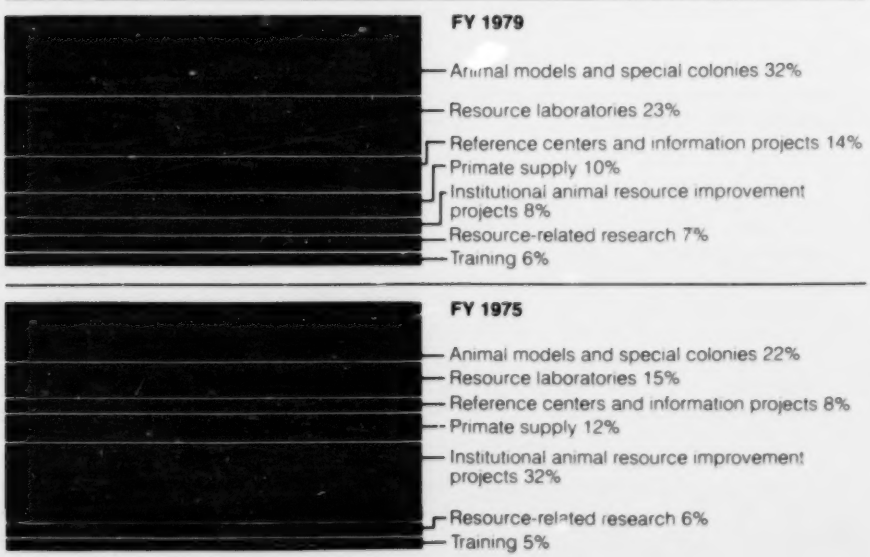
During the year, the Animal Resources Program supported six contracts and five grants for the domestic breeding of nonhuman primates, in addition to a contract for a Primate Supply Information Clearinghouse. During 1978 and the first 6 months of 1979, the clearinghouse placed 4,242 primates and located cadavers, blood samples, and tissues for 177 projects. By effectively transferring primates and tissues to and from investigators, the clearinghouse saves about 2,000 primates each year.

The six breeding contracts produce animals for general distribution to NIH extramural investigators, with an ultimate goal of providing 1,200 rhesus monkeys, 150 cynomolgus monkeys, and 400 squirrel monkeys per year by 1986. The squirrel monkey breeding contracts may not meet their goals because of difficulty in obtaining breeding stock, losses due to disease, and reproductive rates that are lower than anticipated. The rhesus and cynomolgus monkey breeding contracts, however, will come close to reaching their goals. In 1979, the breeding contracts provided NIH extramural investigators with 348 rhesus monkeys, 81 squirrel monkeys, and 22 cynomolgus monkeys. In addition, 200 rhesus monkeys were provided to Lederle Laboratories at the request of the Food and Drug Administration for safety testing of polio vaccine. The five grant-supported breeding projects included establishment of a specialized production colony for the endangered species, *Saguinus oedipus* (cotton-topped marmoset); one for owl monkeys; one for baboons; and two for several other species of marmosets.

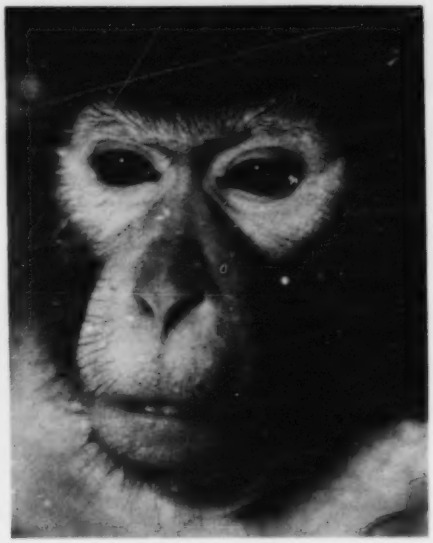
**Laboratory Animal Sciences Program**

Projects supported by the LASP achieved their overall goals of providing researchers with healthy research animals and improving animal research facilities in 1979. Four new

**Funded Project Areas Comprising the Total LASP Budget for FY 1975 and FY 1979**



*Studies on aging conducted at the Delta Primate Research Center this year suggest that cellular pigment may be linked to the aging process. The 8-year-old monkey (near right) has an age equivalent to 24 human years, while the 28-year-old monkey (far right) has an age equivalent to 84 human years.*



*LASP-supported animal model projects this year encompassed a broad spectrum of research models, including congenic mice (above).*

*The Laboratory Animal Sciences Program supported 17 animal model and special colony projects this year, including a Gulf Coast squid resource (below). Because of their large axons, certain species of squid are excellent for studies of nerve impulses and synaptic transmission.*

proposals were funded for institutional animal resource improvements this year, bringing the total to seven projects supported with $709,000 (11 percent of the LASP budget). These projects provided updated equipment, renovation, and general improvement of animal facilities. Data from a "Survey of Laboratory Animal Facilities and Resources" indicate an ongoing need in this area, and limited numbers of improvement projects will continue to be funded.

Seventeen animal model and special colony projects were supported during the fiscal year. They constituted 34 percent of the LASP budget at $1.382 million and included two new resource grants for a multidisciplinary effort to identify, characterize, and make available new animal models of human genetic diseases and for a study to develop techniques for culturing the sea hare, *Aplysia californica*. The sea hare is a well-established model for neurophysiological and behavioral research. Its use in past research was limited by decline in the wild population and the difficulty of maintaining the species in captivity.

Other 1979 activities were primarily directed toward use of vertebrate animals, including a rabbit inbred and mutant stock resource, a mouse mutant gene resource, a congenic mouse resource, and two hamster resources. The animal model projects encompassed a broad spectrum of research models, including use of the squirrel monkey as a model for the effects of noise on hearing, use of garter snakes to study neuronal aging, and use of the Brittany spaniel to study hereditary canine spinal muscular atrophy.

During the fiscal year, LASP funds also supported 15 resource laboratories, including 1 new laboratory for studies in research animal disease problems. Support amounting to 7 percent of the LASP budget was provided to 10 resource-related projects. Representative projects included the diagnosis and control of mammalian encephalitozoonosis, development of diagnostic/control methods for canine brucellosis, updating of nutrient requirements for rats, and control of respiratory mycoplasmosis in rodents.

Finally, the Laboratory Animal Sciences Program funded 8 active training programs in laboratory animal medicine in 1979, with 29 funded trainee positions and 1 individual postdoctoral fellowship.

## Future Program Directions

In the 1980's, program administrators believe, the program will face continuing scarcity and high costs of primates, an inadequate number of trained laboratory animal specialists, and the need to renovate or replace facilities. In response to these challenges, the program plans to increase domestic breeding of primates, continue funding for institutional improvement projects, and strengthen its research training programs.

**Primate Research Centers Program**

Through its Primate Research Centers Program, the ARP will strive to increase breeding of primates for center use, with the goal of reaching self-sufficiency by the mid-1980's. Steps will be taken to improve each center's scientific productivity by retaining experienced core staff who are well acquainted with the center's research mission, and to

improve the physical plant and equipment to meet the accreditation standards of the American Association for Accreditation of Laboratory Animal Care. While the current number of centers is adequate to assure reasonable access by major groups of U.S. scientists, use of centers will be extended by increasing the opportunities for outside investigators to work within the centers on a short-term basis.

**Primate Breeding and Resources Program**

Other primate resources supported by the Animal Resources Program will step up primate breeding to assure a stable supply of essential primates for NIH extramural research. The ARP will breed commonly used primate species that cannot be obtained in sufficient numbers from wild populations: the chimpanzee, used to study behavior,

*The first baby baboon* (Papio anubis) *born at the Oregon Primate Research Center. Through its Primate Research Center Program, the Animal Resources Program will strive to increase breeding of primates for center use with the goal of reaching self-sufficiency by the mid-1980's.*

*The Laboratory Animal Sciences Program in the eighties will give priority to developing animal models and colonies useful to a broad group of user scientists. This Abyssinian guinea pig from a LASP-supported animal diagnostic laboratory offers a model for diabetes mellitus.*

learning, and infectious diseases; the rhesus monkey, which for years has been the standard laboratory primate; and the cynomolgus monkey, often used to replace the rhesus monkey.

In its attempt to fill the gap between need and supply, the program will continue to seek out other potentially useful species. It will also establish better breeding methods to solve problems that have arisen in breeding large groups of some primate species—such as owl monkeys—in captivity. The ARP will continue to encourage shared use of primates and continued funding of the Primate Information Clearinghouse.

**Laboratory Animal Sciences Program**

The Laboratory Animal Sciences Program in the eighties will focus on developing higher quality institutional animal resource programs. It will also develop animal models as needed by the NIH Institutes and will give priority to development of animal models and colonies with a broad user base.

LASP resource laboratories will continue to monitor and implement quality control procedures for identifying naturally occurring laboratory animal diseases that can invalidate biomedical research results. The LASP will also support in-depth studies of laboratory animal diseases and their etiology.

Finally, training programs will be expanded to combat the anticipated shortage in the eighties and nineties of veterinarians with postprofessional education. Many attractive positions in laboratory animal science now go unfilled for long periods of time. To alter this situation, the program plans training groups at educational institutions and programs to employ veterinary students during the summer as an incentive to postdoctoral, research-oriented careers.

# Minority Biomedical Support Program

## Program Description

Although ethnic minority groups comprise more than 18 percent of this country's total population, in 1977 they constituted only 2 percent of all persons employed in the health-related sciences. The limited involvement of minority institutions in biomedical research discouraged minority students from entering the field and placed those who did at a competitive disadvantage when they applied for advanced training. Moreover, faculty members at minority institutions were frequently unable to engage in research because of heavy teaching loads and lack of necessary facilities and equipment.

To correct the underrepresentation of minorities in biomedical research and to eliminate obstacles to their participation, the DRR Minority Biomedical Support (MBS) Program was begun in 1972. The major thrust of the program is to develop minority student, faculty, and institutional involvement in biomedical research. Through its grants, the MBS Program supports projects designed to strengthen the biomedical research capabilities of minority institutions and to expand the involvement of minority faculty and students in biomedical research. Funds are provided for scientific equipment, facility renovations, improvement of animal care facilities, support of students, travel to professional meetings, and release of faculty from teaching to conduct biomedical research.

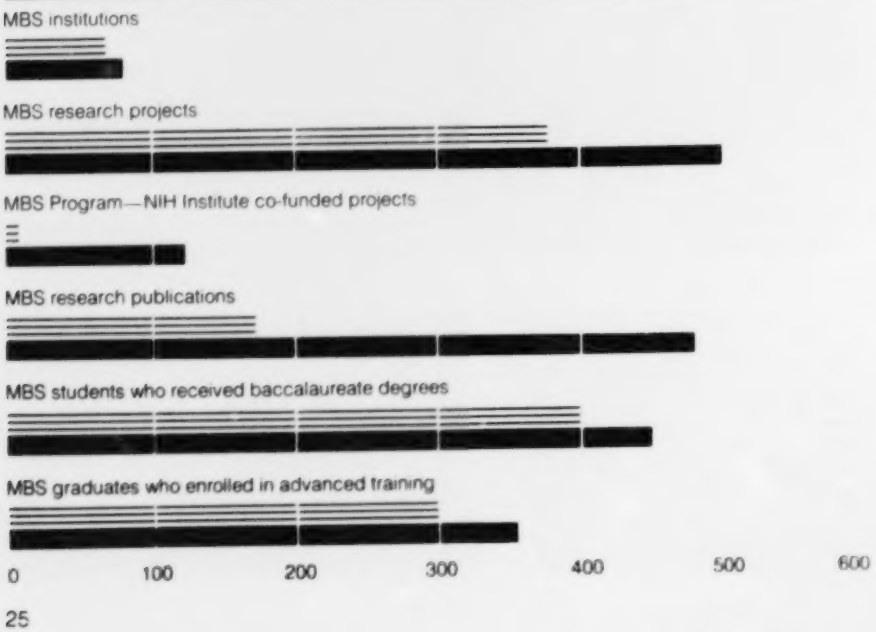
## Program Growth

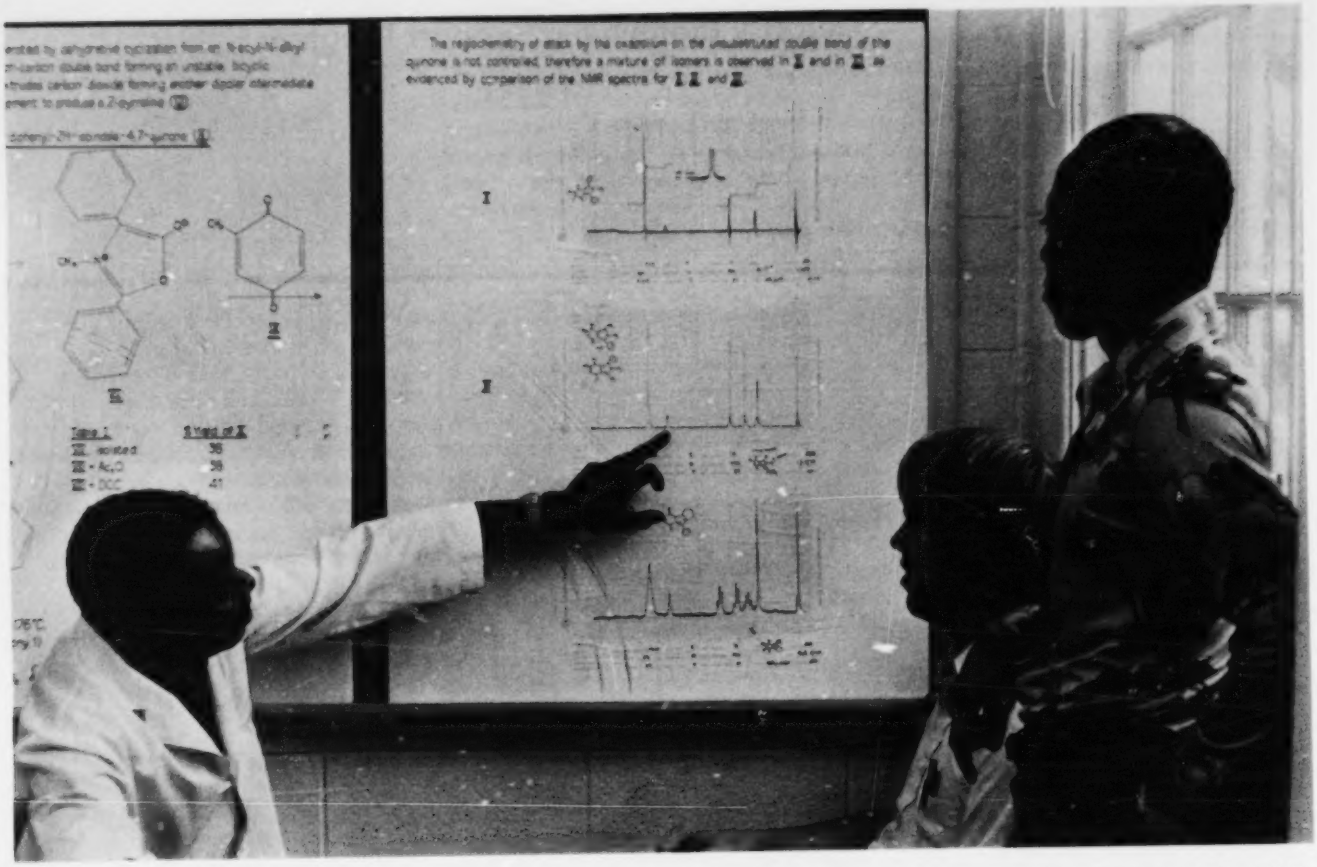
The MBS Program has steadily increased the number and types of institutions and the scope of projects supported. At its inception in 1972, the program supported 170 research projects at 38 institutions; in 1979, it supported 500 projects at 80 institutions. Unlike the original 38 institutions, the 80 institutions now supported include 2-year colleges. Most have large minority student enrollments.

The scope of program support has branched out from general institutional support for facilities and personnel to encompass funding for individual research projects involving faculty and students. A unique feature of the program is its emphasis on undergraduate participation in all aspects of biomedical research, from conceptualization of important research questions to design of experiments, review of the literature, collection and analysis of data, and finally, the interpretation and reporting of results at meetings and in scientific journals.

Through its cooperative agreements with nearly all 11 Institutes of the NIH and the

## Minority Biomedical Support Program Accomplishments





*Synthesis of radiosensitizer compounds, which enhance radiation cancer therapy in mice by increasing damage to cancer cells, resulted from a joint effort by two MBS institutions in 1979. Here an investigator points out a structural property of one of the compounds that he and the investigator on the far right synthesized.*

*More students are participating in and graduating from the MBS Program. Here Dr. Ciriaco Gonzales (center), director of the MBS Program, discusses research opportunities with two students during the 1979 MBS Symposium in Atlanta, Georgia.*

National Institute of Mental Health, the program has become the cornerstone of the NIH's extramural affirmative action program. Agreements between the Institutes and the MBS Program began in 1974 when the Director of the National Institutes of Health requested that all Bureaus, Institutes, and Divisions initiate and coordinate minority program activities through the existing minority programs, i.e., the Minority Access to Research Careers Program of the National Institute of General Medical Sciences and the DRR Minority Biomedical Support Program. The purpose of these intra-agency agreements is to provide MBS investigators with the opportunity to participate in areas of research sponsored by the various NIH institutes. The MBS Program staff identifies research projects that appear to fit each Institute's mission. If the Institute approves the project and has funds available to support it, the MBS Program then acts as a clearinghouse and managing unit.

By becoming acquainted with the Institute's research thrust and grant application requirements, MBS institutions and investigators can compete equally for future Institute grants via the normal application route. In this way, the intra-agency agreements have augmented MBS Program efforts to help ethnic minority scientists enter the mainstream of the nation's biomedical research effort. These agreements have also broadened the financial support base for minority biomedical research. In 1972, no intra-agency agreements existed. In 1975, eight projects were funded for $341,964 through two agreements. Currently, Institutes have agreements with the MBS Program to fund 114 research projects for a total of $4,564,705.

The MBS Program has grown in other areas as well. MBS-supported research activity has become more productive. More students are participating in and graduating from the program, and the research capability of MBS institutions has significantly improved. The 1979 research at one MBS institution resulted in development of an RNA fingerprinting technique to analyze the unusual arrangement of genetic information in four different RNA molecules of three plant viruses. Research at another MBS institution this year may lead to development of a vaccine for schistosomiasis. The potential vaccine is currently being tested in rhesus monkeys. In addition, a joint effort by two MBS institutions resulted in a method to enhance radiation in cancer therapy involving mice. Compounds called radiosensitizers developed at one institution were tested at another institution, and were found to increase radiation damage to cancer cells in mice.

One indication of this increased research productivity is the greater number of papers presented by MBS students and faculty at scientific meetings. MBS students made 439 presentations at scientific meetings in 1979, compared with 212 in 1974, and MBS faculty investigators made 356 presentations at scientific meetings in 1979, compared with 143 in 1974. Investigations by MBS faculty and students resulted in 502 research publications in 1979, compared with 75 in 1974.

This increased productivity arose in part from the growing number of students participating in the program. In 1972, only 282 undergraduates and 45 graduate students participated in the program; by 1979, 910 undergraduates and 329 graduate students participated. From 1972 to 1979, a total of 2,878 MBS students graduated with bachelor's degrees. Of these, 799 entered medical schools, 150 entered dental schools, 775 entered other graduate schools, 417 entered health-related schools, and 677 entered other careers.

## Program Highlights for the Year

This year marked the continued entry of minority scientists and students into biomedical research. A number of faculty investigators won NIH grants through the national competitive application process. Twenty-eight MBS investigators were appointed to NIH scientific review committees or advisory groups and one to the Recombinant DNA Advisory Committee. Thirty graduates of MBS-supported Ph.D. programs are now doing postdoctoral work at major laboratories, and many more minority students and faculty are participating in biomedical research. The MBS Program funded positions for 402 faculty, 739 undergraduate, and 247 graduate students in 1979.

One of the year's major highlights was the Annual MBS Symposium held in Atlanta, Georgia, in April. The majority of the 1,500 individuals who attended were student investigators. Many scientific papers were presented by minority students, and several invited papers were presented by well-known scientists, including two Nobel laureates. The symposium included workshops on scientific techniques such as isoelectric focusing with polyacrylamide gel, radioimmunoassay, liquid chromatography, liquid scintillation counting, and computer graphics. A number of institutions sent representatives to the symposium to provide minority students with advice on their graduate and professional programs, and several NIH representatives attended to explain NIH application guidelines.

Two changes in MBS procedure enhanced the program's effectiveness. For the first time, 2-year colleges became eligible to submit applications for MBS funding, and two such colleges were funded this year. Secondly, the PROPHET system—a set of computerized tools for data management, graphical and statistical analysis, curve fitting, and mathematical and molecular modeling—was made available to MBS institutions through a new agreement with the DRR Biotechnology Resources Program. Under this agreement, at least one PROPHET user site per year will be established at an MBS institution. The first PROPHET workshops and demonstrations will be conducted during 1980.

## Future Program Directions

In the 1980's, the program will give priority to development of minority faculty and institutions. However, more opportunities will be provided for undergraduate summer training at other institutions and for graduate training.

Future opportunities for faculty may include research career awards and postdoctoral fellowships for training in special areas or in a new technology. The institutional research environment of the eighties will be enhanced by continued funding for modern equipment, laboratory space, and animal facilities still lacking in many MBS institutions. Those institutions which have already attained an adequate biomedical research capability will be assisted to obtain funding from non-MBS sources for central resources to maintain that capability.

Photos by Walter Scott

*In the 1980's, more opportunities will be provided for MBS undergraduates (right) to participate in summer research internships.*

# Biomedical Research Support Program

The DRR Biomedical Research Support Program administers two institutional research grant programs, the Biomedical Research Support Grant (BRSG) Program and the Biomedical Research Development Grant (BRDG) Program. The BRSG Program enhances the quality and productivity of biomedical research at the nation's largest research institutions, and the BRDG Program assists new, small, or developing institutions to expand and strengthen their health-related research.

## Biomedical Research Support Grant Program

For biomedical research at the nation's largest research institutions to be productive, a source of funding must be maintained for short-term, emergency, low-cost, interim, shared research resource needs not covered by other PHS research grants. An investigator may need to learn a new skill or technique, a promising project may be in danger of interruption between grants, a new idea may require pilot research, essential equipment may break down, or new equipment may be needed to continue research. Often, these needs are not specified for funding by other PHS grants or cannot be provided in time by those grant mechanisms. To fill these gaps, the Biomedical Research Support Grant Program (formerly the General Research Support Grant Program) was authorized in 1960.

Unlike most grants, BRSG grants are designed for flexible use at the discretion of the grantee institution. One institution may use BRSG funds for shared equipment. Another institution may have funds for shared equipment but may need BRSG funds to support new investigators or pilot research. However, all BRSG funds are intended to complement or supplement other types of PHS research grants; for instance, an investigator with a new or unexpected research cost not adequately met by a project grant can submit a request for BRSG funds to the BRSG program director at that institution. Advice on the merits of each request is provided to the program director by appropriate scientific and administrative staff of the institution. The program director then selects for funding those projects that best improve research at the institution.

BRSG funds may also complement awards for biomedical research made by non-PHS agencies such as the National Oceanic and Atmospheric Administration, the Environmental Protection Agency, and the U.S. Department of Agriculture. In one such case, the National Science Foundation recently funded a centralized amino acid analyzer facility, which serves two different institutions. Each institution provides funds for staff and supplies for the first 2 years of operation. One institution used BRSG funds for this purpose. After the initial 2 years, the facility will be supported by funds from a core of user scientists.

The objectives of the BRSG Program are to enhance the quality, increase the productivity, and reduce the cost of biomedical research at the nation's large research organizations, health professional schools, other academic institutions, and hospitals. It accomplishes this in several ways. For example, pilot studies test the validity of new ideas and the feasibility of research methods to be used in a particular study. This reduces the risk of major cost commitments to projects that might be unproductive and, at the same time, encourages innovation. BRSG funds for new investigators, including minorities and women, enable them to set up laboratories, conduct initial research, and gain post-training research experience. By supporting a promising investigator to begin research immediately after completing training, an institution ensures that the investigator's skills and knowledge will remain current and will contribute to the biomedical capability of the institution.

BRSG funding of emergency and interim needs also saves research projects from being interrupted or abandoned before completion. Occasionally, a research project requires redirection, the collaboration of other investigators, or the acquisition of skill in a new or unfamiliar technique. Funding also becomes critical during temporary interruption of PHS project grant support, which can force professional and technical personnel into other activities, making them unavailable when project funding resumes. BRSG funding at

*BRSG Program funds enable biomedical scientists to take advantage of research opportunities which would otherwise be lost. On the opposite page a researcher observes cells migrate from biopsy fragments and begin dividing to start new cell lines.*

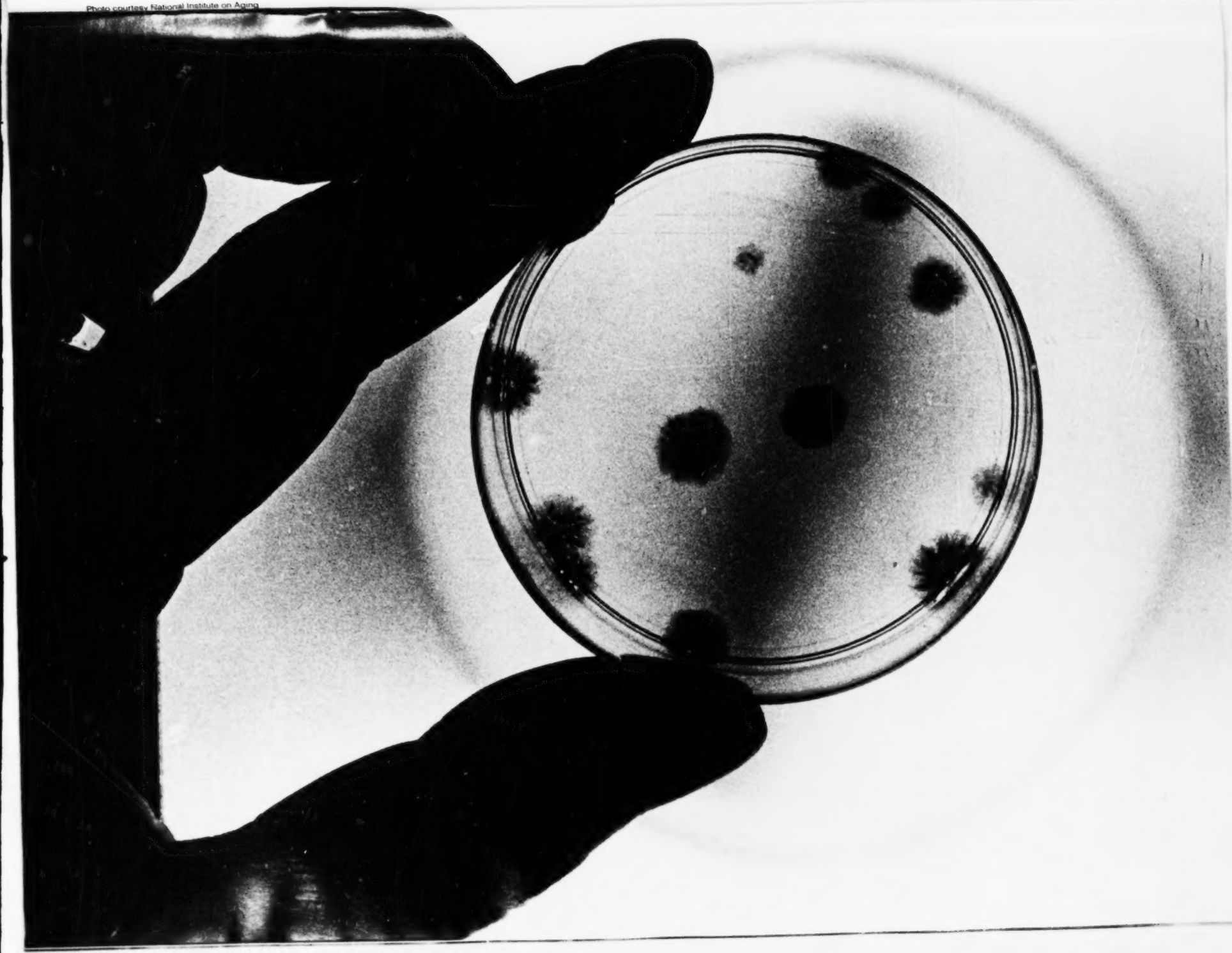


Photo courtesy National Institute on Aging

*Transmission electron micrograph reveals cross-sections of microtubules arranged in circular bundles at the periphery of discoid blood platelets. BRSG-supported research in 1979 resulted in improved blood bank storage conditions which preserve microtubules, enabling them to retain their platelet-shaping function. This preserves normal platelet shape and capability for circulating properly after blood transfusion.*

Photo courtesy of Dr. Manley McGill, American Red Cross Blood Services, Bethesda, Maryland

this point keeps the staff on the project and prevents the need for costly reassembly and training of a new research team when project grant support is resumed.

Finally, BRSG funds are used to support shared equipment not appropriately funded by other sources; for example, several investigators may need the same instrument for their individual projects. Program support of this shared equipment minimizes research costs by avoiding equipment duplication at the institution and by reducing the time required to complete certain phases of a project through use of this equipment. Furthermore, the overall quality of research is enhanced—this equipment may answer important questions that otherwise could not have been investigated, or it may improve the precision and reliability of findings.

**Program Growth**

The complementary and supplementary role of the BRSG Program has become increasingly important to sustaining the nation's biomedical research effort in the current climate of increasing research costs and reduced budgets for funding research. These conditions have resulted in greater competition for BRSG funds at grantee institutions. At the same time, the maximum dollar amount of individual BRSG awards has also declined from $420,000 in 1969 to $201,000 in 1979. Yet, the number of institutions receiving maximum BRSG awards (institutions with more than $6 million annually in PHS research grants) has increased from 10 in 1970 to 58 in 1979. Although competition for funds within each institution has intensified, more institutions are being assisted. More than 9,500 PHS research projects currently receive direct BRSG support. An undetermined number of projects are supported indirectly through BRSG-funded, centrally shared equipment, resources, and facilities.

**Program Highlights for the Year**

During the last reported 12-month period, the BRSG Program funded 5,098 pilot projects and 4,467 regular projects. It provided support to 2,274 new investigators, 801 minority investigators, 2,164 students, and 1,380 women, and it assisted 775 relocated investigators to resume research in their new location. Program support resulted in 4,864 research publications and in applications which competed successfully for 1,605 other research grants. This discretionary use of flexible BRSG funding by the best and largest U.S. biomedical research institutions led to research advances which otherwise would not have taken place.

☐ Preliminary data on a new antitumor drug resulted from BRSG support to a young investigator. On the basis of his initial studies, the investigator won substantial funding from the National Cancer Institute and the American Cancer Society and within a year had developed the drug chlorozotocin. It is effective against malignant tumors, does not damage vital bone marrow, and may prove useful for intensive chemotherapy. Initial clinical tests of the drug in 35 volunteer cancer patients have already begun.

☐ Interim support provided by the BRSG Program enabled a longitudinal study of hepatitis B virus among natives of the Solomon Islands to continue uninterrupted when NIH grant funding was delayed by relocation of the principal investigator. This native population presented a unique opportunity to learn how factors such as heredity, culture, and environment affect virus transmission because the prevalence of asymptomatic virus carriers in this group is 100-fold higher than in the U.S. population. BRSG funding was terminated when the delayed grant was received.

☐ A centralized automatic gamma counter was purchased with BRSG funds. The equipment was used in a study of newborn children to detect thyroid hormone deficiency, which, if untreated, causes permanent mental retardation. Thyroid deficiency was detected in eight infants, and early treatment resulted in normal growth and mental development. Followup support of the project will continue with a 4-year PHS research grant of over $200,000.

**FY 1979 Biomedical Research Support Grants by Type of Institution**

| Type of Institution | No. of Grants | Amount |
|---|---|---|
| Schools of medicine | 109 | $16,053,199 |
| Other health professional schools | 71 | 3,830,688 |
| Other academic institutions | 147 | 12,315,618 |
| Hospitals | 61 | 4,468,569 |
| Health departments | 2 | 57,191 |
| Research organizations | 67 | 5,025,849 |
| | 457 | $41,751,114 |

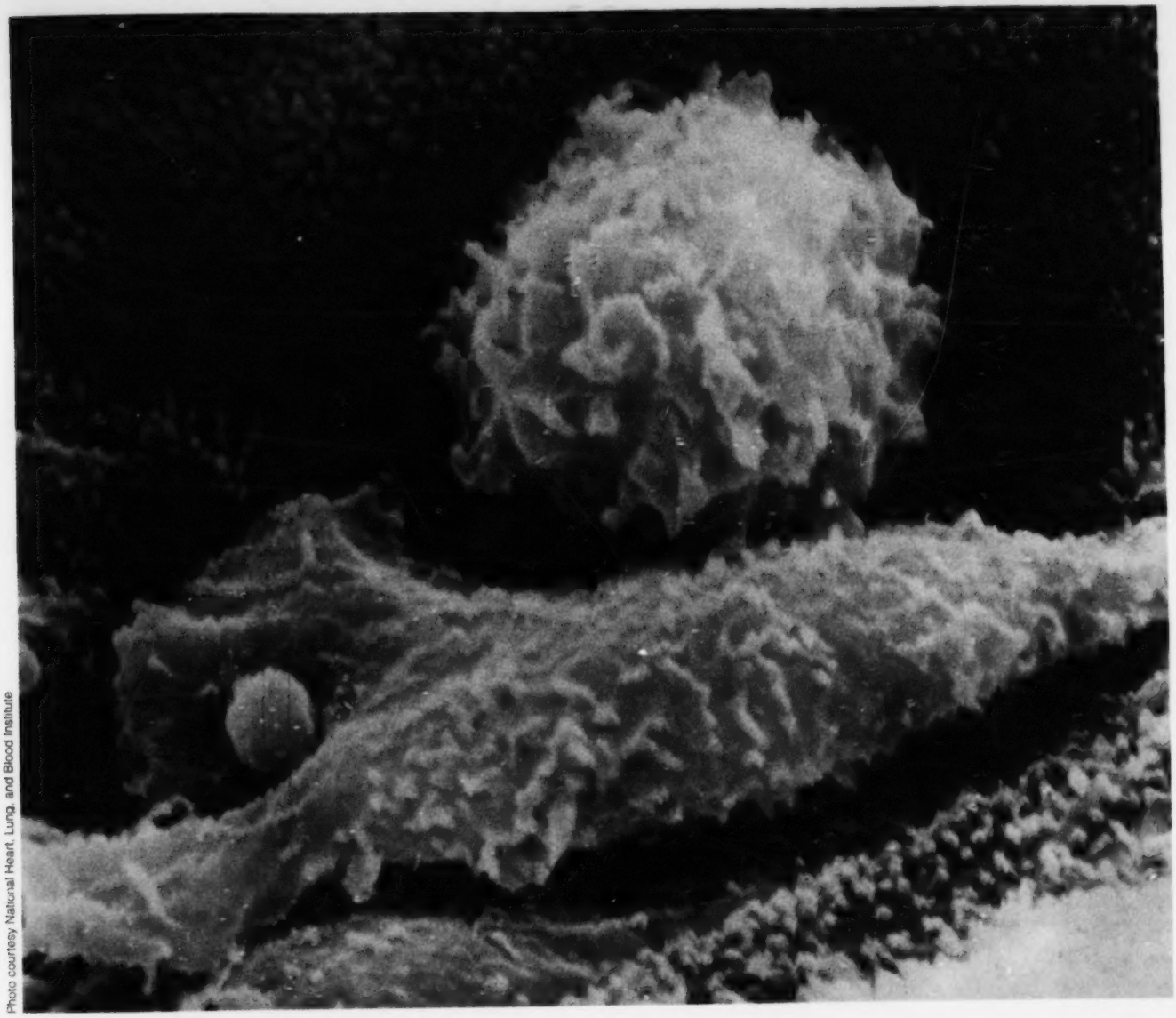


Photo courtesy National Heart, Lung, and Blood Institute

*During 1979, the BRSG Program funded 5,098 pilot projects and 4,467 regular projects, which included research into the production of human interferon by highly purified macrophages. When battling infections, macrophages produce interferon. Here one of two macrophages (bottom) devours a foreign particle.*

□ BRSG funds were also used this year to supplement other research funding sources; for example, program funds were used to supplement NIH funds for the study of periodontosis, a severely destructive disease that causes rapid loss of tooth-supporting bone in adolescents, often resulting in tooth loss before the age of 25. The use of BRSG funds accelerated research in the use of new techniques to culture air-sensitive microbes, leading to findings that the disease was caused by a hitherto unidentified bacterium that can be controlled by antibiotic therapy. BRSG support in this case shortened the time needed for a dramatic change in the understanding of this baffling disease.

**Future Program Directions**

This BRSG Program will play an increasingly critical role in supporting U.S. biomedical research in the eighties, particularly if PHS research funds continue to fail to keep pace with the rising costs of research. Institutions will need BRSG funds more than ever as emphasis shifts from center grants, which usually include some core support, to research project grants, which do not. At the same time, funds appropriated to the BRSG Program will continue to decline from 2.3 percent of appropriated NIH research grant funds in 1980 to an estimated 2.1 percent in 1981. As a result, competition for limited BRSG funds at grantee institutions is becoming even more acute.

The increased complexity, rapidly advancing capabilities, and higher costs of shared instruments and the declining ability of institutions to fund their capital costs from either BRSG funds or other PHS grants may prompt the program to establish a competitive shared instrument grant program beginning in 1982. This program would respond

*Cluster of fat cells magnified 300 times by a million-volt electron microscope at a DRR biotechnology resource facility. Such DRR-supported research resources broaden researchers' knowledge of metabolism and the body's other intricate processes.*

selectively to equipment needs wherever they exist and would free more BRSG funds at those institutions for other research needs.

Another priority in the early eighties will be improved measurements of the program. Important accomplishments have been identified; however, the full impact of the program has not yet been fully assessed. Most program activities affect not only the institution per se, but also investigators' careers, the progress of research projects, and the advancement of health knowledge in general. More analytical measures of these benefits need to be developed.

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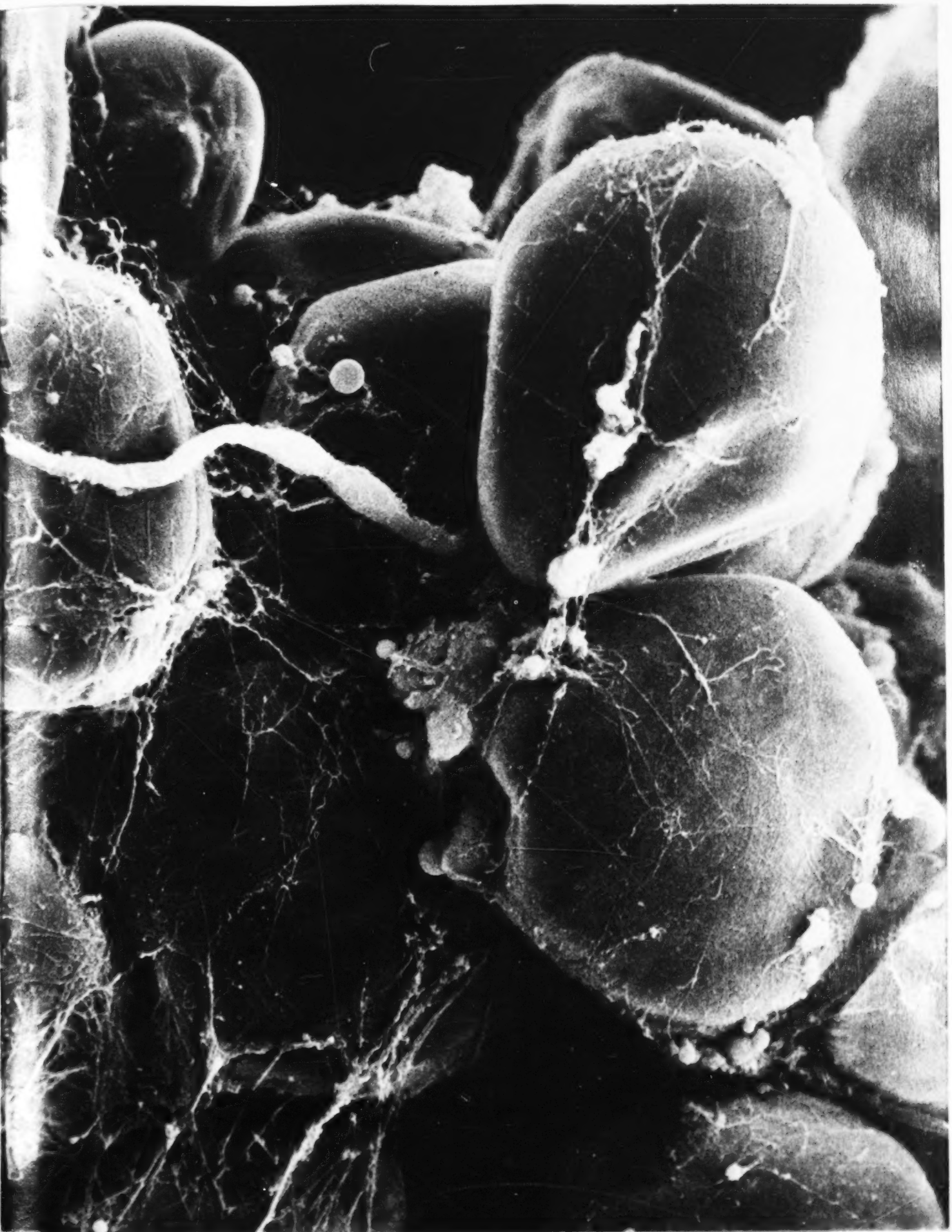
**Biomedical Research Development Grant Program**

In 1977, the Biomedical Research Development Grant Program was established to provide grants on a competitive basis to institutions engaged in health manpower training that receive less than $200,000 a year in PHS research grants. Up to 10 percent of BRSG funds were made available to the BRDG Program to expand and strengthen health-related research at such new, small, or developing research institutions. Awards are made for a maximum of 3 years and for not more than an average of $100,000 per year. The program provides funds to hire new research personnel, improve the research skills of existing personnel, set up new laboratory space, purchase needed research equipment and supplies, provide release time from teaching and other nonresearch duties, establish shared central research resources, acquire consultant services, and finance appropriate travel.

Since its inception the program has succeeded in developing such high-quality research at these institutions that they have won other research support. 12 original grantees have acquired a total of $2.6 million dollars in funding from other agencies. After only 1 year of BRDG support, 3 of the 12 institutions qualified for BRSG support, which is limited to institutions receiving a minimum of $200,000 in PHS research grants in 1 fiscal year.

Although these institutions have benefited from the program, continuing need for the program is diminishing. Fewer applications are being received each year, with the majority coming from previously unsuccessful applicants. Therefore, the program will be phased out over the next 3 years as periods of committed support expire. The BRDG funds will be returned to the BRSG parent program, and may be used in the proposed shared instrument grant program.



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